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Environmental Cancer and Heart and Lung Disease - Fifth Annual Report to Congress

Technical Resources, Inc.
Bethesda, MD

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ENVIRONMENTAL CANCER AND HEART AND LUNG DISEASE

FIFTH ANNUAL REPORT TO CONGRESS

August 1982

TASK FORCE ON ENVIRONMENTAL CANCER AND HEART AND LUNG DISEASE

U.S. Environmental Protection Agency • National Cancer Institute
National Heart, Lung, and Blood Institute • National Institute for Occupational Safety and Health
National Institute of Environmental Health Sciences • National Center for Health Statistics
Centers for Disease Control • Food and Drug Administration

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The Fifth Annual Report to Congress describes the activities of the Task Force on Environmental Cancer and Heart and Lung Disease between September 1981 and August 1982. The Task Force recommendations to Congress are: (1) continued operation of the National Death Index under NCHS, (2) development of effective procedures to minimize or remove legal impediments to epidemiologic research at both the Federal and non-Federal levels, and (3) promotion of the education of medical and other health care students and practitioners in environmental disease prevention through the coordination of efforts and joint initiatives by the professional medical organizations and Federal Agencies. Also included in the report are brief overviews of selected current assessments of the link between environmental factors and human cancer, heart disease, and lung disease. Current Federal activities in disease prevention are summarized, and an update of the environmental disease research activities and research priorities of each member Agency is provided. The full scope of Working Group and Project Group activities are described and future directions are suggested.

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TASK FORCE ON
ENVIRONMENTAL CANCER AND HEART AND LUNG DISEASE

Please address your reply to:

John W. Hernandez, Jr., Ph.D.
Deputy Administrator
U.S. Environmental Protection Agency
Washington, D.C. 20460

November 15, 1982

Honorable Thomas P. O'Neill, Jr.
Speaker of the House of Representatives
Washington, D.C. 20515

Dear Mr. Speaker:

As Chairman of the Task Force on Environmental Cancer and Heart and Lung Disease, I am pleased to submit to you the Fifth Annual Report to Congress in accordance with Public Law 95-95, Section 402(b)(5).

The eight member Agencies, which constitute the Task Force, continue to work together to investigate possible relationships between environmental pollutants and human disease. This report includes brief summaries of some of the current information on the relationship between environmental factors and human cancer, heart disease, and lung disease. In addition, each member Agency has provided the Task Force with an overview of their respective Agency's research activities in these areas, including their identified research priorities for the future.

The elucidation of cause-and-effect relationships between environmental pollution and human disease is an almost impossibly difficult scientific problem. Interagency cooperation and coordination, which are integral to this particular Task Force, provide a useful approach in addressing promising aspects of this problem.

I am personally gratified by the active participation of the member Agencies from the Department of Health and Human Services. You should know that all of the participants of the Task Force have worked hard and have openly cooperated during the past year. I look forward to continuing our work together to improve our understanding of environmental factors and human disease.

Sincerely,

John W. Hernandez, Jr.
Chairman

Environmental Protection Agency • National Cancer Institute
National Heart, Lung and Blood Institute • National Institute for Occupational Safety and Health
National Institute of Environmental Health Sciences • National Center for Health Statistics
Centers for Disease Control • Food and Drug Administration

TASK FORCE ON
ENVIRONMENTAL CANCER AND HEART AND LUNG DISEASE

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John W. Hernandez, Jr., Ph.D.
Deputy Administrator
U.S. Environmental Protection Agency
Washington, D.C. 20460

November 15, 1982

Honorable George Bush
President of the Senate
Washington, D.C. 20510

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PREFACE

The Task Force on Environmental Cancer and Heart and Lung Disease is an interagency group established by Congress through the enactment of Section 402 of Public Law 95-95, the Clean Air Act Amendments of 1977. The Task Force is mandated to determine and quantify the relationship between environmental pollutants and human disease and to recommend and coordinate Federal research programs aimed at reducing or preventing the incidence of environment-related cancer and heart and lung disease. The Task Force is also mandated to stimulate cooperation among member Agencies. Although such cooperation has existed for some time, the formation of the Task Force formalized and intensified the cooperation between the U.S. Environmental Protection Agency and various components of the Department of Health and Human Services.

The Task Force member Agencies are the U.S. Environmental Protection Agency (EPA) and, within Health and Human Services (HHS), the National Cancer Institute (NCI), the National Heart, Lung, and Blood Institute (NHLBI), the National Institute for Occupational Safety and Health (NIOSH), the National Institute of Environmental Health Sciences (NIEHS), the National Center for Health Statistics (NCHS), the Centers for Disease Control (CDC), and the Food and Drug Administration (FDA). The Administrator of the EPA (or a person delegated by the Administrator) chairs the Task Force. The Task Force is required to report annually to Congress on its progress in quantifying the relationship between environmental pollutants and cancer and heart and lung disease.

This report describes the activities of the Task Force between September 1981 and August 1982. Chapter 1 presents a review of the Task Force's first 4 years and a brief status report on fifth-year activities. Chapter 2 states the Task Force recommendations to Congress. Chapter 3 gives brief overviews of selected current assessments of the link between environmental factors and human cancer, heart disease, and lung disease. Chapter 4 summarizes current Federal activities in disease prevention. To update information contained in the First Annual Report, Chapter 5 describes the environmental disease research activities and research priorities of each member Agency. Chapter 6 describes the full scope of Task Force activities for the year and outlines future directions.

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EXECUTIVE SUMMARY

Congress established the Task Force on Environmental Cancer and Heart and Lung Disease to recommend research to determine and quantify the relationship between environmental factors and human disease and recommend strategies, research, and other measures to prevent or reduce the incidence of environmentally related diseases. The three disease endpoints chosen as the Task Force focus are dominant in American public health--heart disease is the leading cause of death, cancer second, and lung disease (chronic obstructive pulmonary diseases) fifth. Both experimental and clinical observations have suggested associations between the occurrence of these diseases and environmental factors.

The Task Force reports annually to Congress on its progress. This Fifth Annual Report presents the progress of the Task Force in implementing its mandate and the progress of the member Agencies in environment-related disease research.

Five years of Task Force activities have provided the means for sustained dialogue and exchange of information and cooperation between the Public Health Service Agencies within HHS and EPA, which are those Federal Agencies most directly concerned with the study of the environment and human health. The Task Force has undertaken various types of activities--workshops, publications, inventories of research, formulation of recommendations--relevant to the determination of the relationship between the environment and disease. The problem of linking environmental factors and human disease is scientifically complex, and, in fact, definitive data exist for only a handful of cases.

As part of its effort to identify gaps in environmental disease research, the Task Force this year compiled brief summaries of selected assessments of the relationship between environmental factors and human cancer, heart disease, and lung disease. Except in a few instances, usually characterized by a unique exposure and rapid pathological response, cause-and-effect relationships between environmental pollution and human disease have not been established.

The Task Force, as an interagency body, and its eight member Agencies, individually, continue working toward the elucidation of environment-disease relationships. A few of the recent advances in three broad areas relevant to this problem include the following:

- Exposure assessment
  - Development and evaluation of new methods for assessing dose-effect relationships
  - Development of new analytical techniques for separating, detecting, and measuring toxic substances
  - Improved methodology for investigating effects of low levels of pollutants in humans
- Extrapolation of animal data to humans
  - Development of pulmonary function measurement techniques so that most pulmonary functional tests that are important in humans can be performed in small animals
  - Development of animal models for human breast, ovarian, colon, pancreatic, prostatic, and bladder cancer
  - Development of animal models for assessing reproductive effects
  - Development of mathematical models to translate animal data into estimates of human risk

- Mechanisms of disease
  - Demonstration that human cells and tissues in culture show qualitative patterns of metabolism of carcinogenic chemicals similar to those of animal cells and tissues known to be sensitive to the carcinogenic effects of the chemical
  - Prediction of mutations by research on cloning and molecular characterization of genes.

Other important advances continue to result from basic laboratory research, exposure monitoring, epidemiological studies, occcupational hazards and disease surveillance, field studies of disease outbreaks and hazard situations, disease screening programs, national health surveys, and monitoring of foods, drugs, cosmetics, and medical devices. For this report, each Task Force Agency has provided an overview of its research programs and enumerated some recent findings and advances in environment-related disease research.

This information is presented as part of the continuing process through which the Task Force seeks to identify gaps in environmental disease research. A major Task Force activity to facilitate this process is a workshop on environmentally related nononcogenic lung diseases. This subject was chosen because it is an important aspect of the Task Force's mandate about which relatively little is known. The workshop, planned for FY83, will bring together experts in this area from the scientific community. The subject emphasis will be air pollution with lung as the target organ. The workshop will be designed to describe the present state of knowledge, as reflected by basic and animal research, clinical studies, and epidemiology and health data banks. Workshop participants will examine what needs to be known and, on the basis of the gaps in information, will develop research recommendations.

Other current Task Force activities are in the areas of quality assurance in analytical methodology, the assessment of human exposure to pollutants, extrapolation of animal data to humans, and environmental health information resources for the education of health professionals. The Task Force plans to formulate recommendations for research that will help fill in gaps in our information base.

This first recommendation of the Task Force to Congress is a reiteration of support for the National Death Index. Last year's report recommended the implementation of the NDI, a central, computerized index of death record information. The NDI is now operational, and the Task Force considers that support to the NDI is especially important during its early years of existence. The NDI contains information investigators can use to tell if persons in their studies have died and if deaths are confirmed, the investigator can then write to the state for the death certificate, which lists the cause of death. This information is extremely valuable to prospective epidemiological research, particularly large studies of several thousand individuals. The NDI will be increasingly useful to retrospective studies as more years of death are added to the file.

The second recommendation is also a reiteration of a recommendation in the Task Force's Fourth Annual Report. The Task Force considers that elimination of legal impediments to epidemiologic research is essential to the study of the link between the environment and human disease. Information on individuals should be available to medical researchers conducting approved studies, with appropriate safeguards to ensure individual privacy.

The third recommendation relates to the Federal policy focus on disease prevention. Health professionals need information about environmental and occupational factors that contribute to disease. Professional medical organizations and certain Federal Agencies should be encouraged to undertake initiatives to promote environmental disease prevention education for medical and other health care students and practitioners.

In the interest of protecting the environment and promoting human health, the Task Force suggests that the following problem areas are among those that constitute research priorities for the determination of the relationship between environment and human disease:

- There is a need to improve our understanding of basic mechanisms through which humans take up, modify, and excrete chemicals
- Improved methodologies for estimating human risk are needed
- Systems are needed to identify and monitor genetic effects in human populations at risk from exposure to hazardous chemicals
- Less resource-intensive methods are needed for assessing the carcinogenic potential of chemicals
- Mechanisms of carcinogenesis, teratogenesis, and mutagenesis require further elucidation
- More reproductive toxicology studies are needed; human mutagenic monitoring systems need to be developed
- Research on environmentally related diseases, other than cancer, should be part of air pollution studies

- New screening methods for hazardous chemicals and faster, more reliable methods for biological effects, such as cardiovascular disease and immune disorders, need to be developed

- More monitoring studies are needed to determine the presence, magnitude, and trends in exposure to environmental pollutants

- Additional epidemiological studies are needed to investigate the relationship between exposure to environmental pollutants and the incidence of human disease.

Chapter 1

INTRODUCTION

HISTORICAL ACTIVITIES OF THE TASK FORCE

The Task Force on Environmental Cancer and Heart and Lung Disease was established by Congress on August 7, 1977, through the Clean Air Act Amendments contained in Section 402(b) of Public Law 95-95.* The mandate of the Task Force was designed to accomplish the following:

- Recommend a comprehensive research program to determine and quantify the relationship between environmental pollution and human cancer and heart and lung disease
- Recommend comprehensive strategies to reduce or eliminate the risks of cancer or such diseases associated with environmental pollution
- Recommend research and such other measures as may be appropriate to prevent or reduce the incidence of environmentally related cancer and heart and lung diseases
- Coordinate research by, and stimulate cooperation between, the Environmental Protection Agency, the Department of Health and Human Services (HHS), and such other Agencies as may be appropriate to prevent environmentally related cancer and heart and lung diseases
- Report to Congress, not later than one year after the date of enactment of this section and annually thereafter, on the problems and progress in carrying out this section.

Representatives from the U.S. Environmental Protection Agency (EPA) and, within HHS, the National Cancer Institute (NCI), National Heart, Lung, and Blood Institute (NHLBI), National Institute for Occupational Safety and Health

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* See Appendix A for full text of section.

(NIOSH), and the National Institute of Environmental Health Sciences (NIEHS) constituted the Task Force. EPA Administrator Douglas Costle chaired the first Plenary meeting of Agency Directors at EPA Headquarters, Washington, D.C., on April 26, 1978. The National Center for Health Statistics (NCHS) and the Centers for Disease Control (CDC) were invited to participate as observers. This meeting provided the forum for the development of objectives and plans and the formulation of a program of activities. A Working Group of alternate Task Force members was established to undertake these activities.*

First Year

The First Annual Report to Congress (August 7, 1978) summarized some of the problems facing the Nation in regard to environmental cancer and heart and lung disease:

- There is evidence that the risk and occurrence of cancer, heart and lung disease increase with environmental pollution, broadly defined to include all environmental factors.
- The extent of illness, death, and costs to society from environmentally related cancer, heart and lung disease is a matter of national concern.
- There is expectation that levels of illness, deaths, and costs resulting from these environmentally related diseases could be substantially reduced by preventive measures.
- Current preventive measures are believed to be inadequate to obtain desired reductions of risk and occurrence.
- Increased knowledge of pollution-disease relations and improvements in strategies and preventive measures are needed for reduction of risk and occurrence.

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* See Appendix B for listing of current Plenary, Working Group, and Project Group members.

- The Federal Government has a central, critical role to take in research and prevention of environmentally related diseases; changes in current Federal efforts may be necessary if desired reductions of risk and occurrence of environmentally related cancer, heart and lung disease are to be obtained.

The Task Force identified six areas of research in which interagency cooperation could assist in resolving environmentally related disease problems. These areas received special Task Force emphasis:

- Standardization of measurements and tests
- Exposure and metabolic mechanisms for pollutants
- Early indicators of disease
- Risk assessment
- Education of the public and health professionals
- Strategies to protect public health.

The report also included information on existing Federal programs that were relevant to the Task Force mission.

Second Year

The Task Force became an eight-Agency group during its second year with the enactment of P.L. 95-623, bringing NCHS and CDC to full membership status. The Food and Drug Administration (FDA) was invited to participate as an observer.

In accordance with the First Annual Report, the Task Force formally established project groups on standardization of measurements and tests, education of the public and of health professionals, and exposure and metabolic mechanisms. One of the first activities of the Project Group on Exposure and Metabolic Mechanisms was to review a feasibility study prepared by NIEHS and submitted earlier to the Task Force. The study was undertaken in relation to a proposed Task Force subject area, early indicators of disease. This report examined the production, use, environmental transport, and metabolic processes of four industrial chemicals, benzene, toluene, carbon disulfide, and methylene chloride. The early indicators of disease subject area was considered to be a subset of the exposure and metabolic mechanisms subject area. The Task Force also initiated the publication of a monthly Calendar of Events, which listed federally and non-federally sponsored meetings, conferences, and workshops dealing with environment and health effects.

The Second Annual Report (August 7, 1979) reviewed the research programs and projects of the Task Force member Agencies in summary and detailed tables, giving categories of research and expenditures for FY78 and estimates for FY79 and FY80. It summarized federally sponsored, environmentally related data bases used for program planning and related activities. The report also included a directory of 21 Federal interagency groups concerned with environmentally related disease, listing the enabling authorization, the chairperson, members, contact persons, and official to whom each committee reported.

Third Year

During its third year, the Task Force voted FDA to full member status; continued monthly publication of the Calendar of Events; produced a preliminary inventory of relevant research programs conducted by member Agencies; and published the second edition of the Directory of Federal Interagency Groups Concerned with Environmental Health.

The Project Group on Education of the Public and of Health Professionals sponsored a workshop, published a summary of the workshop, and developed a full set of recommendations. The Project Group on Exposure and Metabolic Mechanisms analyzed Federal research programs to provide conclusions on needed research and strategies to the Working Group members for the development of recommendations for Agency consideration. The Project Group on Standardization of Measurements and Tests collected information on quality assurance programs of the member Agencies and began a feasibility study on the relationship of laboratory data quality to quality control activities.

The Third Annual Report (August 7, 1980) contained the first set of recommendations from the Task Force. Four recommendations dealt with quantification of the relationships between pollution and disease and the others were developed by the Project Group on Education:

- Multimedia Pollutant Exposure and Health Effects--Research on the relative contribution of various environmental media is needed in order to quantify more accurately the toxicological effects, the risk to human health, and to develop strategies for control of pollutants.

- Transport and Fate of Pollutants in the Biosphere and Food Chain--Research efforts are needed on a comparative analysis of various residuals in air, water, soil, plant, animal, and human tissues. Further studies should evaluate how the pollutant is modified as it moves through the food chain. The development of rapid, inexpensive, and reliable methods for analyzing food contaminants and residuals in biological specimens also is needed.

- Biological and Chemical Measurement Methodology and Data Analysis--Research on methodology of measurements and on data analysis is needed both to assist in the achievement of less expensive study designs and to improve the collection and evaluation of scientific data.

- Pollutants in Groundwater and Surface Water Sources--Comprehensive research should be undertaken to identify the major pollutants in groundwater and in surface water, their persistence and transport, and health effects.

- Interagency Education Program Liaison Group (IEPLG)--Under the aegis of the Task Force, an IEPLG composed of those Federal Agencies that are involved in environmental and occupational health professional education should be established. The mission of this group will be to coordinate and stimulate Federal activities in the area of environmental and occupational health professional education in terms of curriculum, faculty, students, continuing education, and research. The IEPLG will coordinate and assist in implementation of recommendations developed by the Project Group. It will hold conferences and workshops whenever feasible and appropriate. Individuals from outside the Federal Government, including those representing professional societies and organizations, will be invited to participate. The IEPLG will report annually on its activities to the Task Force and to member Agencies on a quarterly basis.

Other education recommendations were related to the development of curricula and curricular models and support for faculty development, postdoctoral and undergraduate training, health professional placement, and research.

Fourth Year

During the fourth year, the Task Force

- Formed the IEPLG

- Published the Directory of Exposure-Related Data Bases

- Continued the feasibility study on the relationship of quality control activities to data quality by the Project Group on Standardization of Measurements and Tests

- Completed a background study on public environmental/occupational health education by the Project Group on Education of the Public and of Health Professionals.

The Task Force also continued publication of the monthly Calendar and maintained and expanded liaison with other interagency groups.

Research needs were identified by the Project Group on Exposure and Metabolic Mechanisms through its January 1981 workshop. The research needs, summarized in the Fourth Annual Report and published in full in a separate document, were oriented to epidemiology, exposure quantification and monitoring, metabolism, in vivo toxicity, and mechanisms of toxicity/carcinogenesis. These needs were directed to the appropriate Agencies for their review and consideration. The Fourth Annual Report (August 7, 1981) also included the following three recommendations to Congress:

- A high priority should be given to the design, implementation, and continued operation of the National Death Index being developed under the auspices of the National Center for Health Statistics.
- Legal impediments to both Federal and non-Federal epidemiology research should be studied further.
- The development of a coordinated environmental health education program for clinicians and health professionals should be fostered.

The introduction of the report presented a brief overview of current trends in death rates, trends in environmental contaminants, and associations between the two. Factors involving cost of disease were also included. The report included summary tables categorizing more than 4,000 Federal Agency projects. Full presentation of inventory data was in three separate reports.

THE TASK FORCE IN ITS FIFTH YEAR

The activities of the Task Force in its first 4 years of existence served to promote interagency coordination and information exchange and develop some specific recommendations for research. That the Task Force has not yet recommended a comprehensive research program to determine and quantify the relationship between environmental pollution and human cancer and heart and lung disease reflects the scientific complexity of the problem of definitively linking (in a cause-and-effect relationship) environmental influences and human disease.

A relationship between human disease and environmental influences, (i.e., factors other than human heredity) has been assumed by most health scientists and biology researchers. This assumption has provided the strong impetus for much of the biological research of recent decades and has been the rationale for research that has led to advances in the fields of physiology, biochemistry, toxicology, and preventive medicine. However, except in a few cases involving unique exposures, experimental exploration has not established the existence of a relationship between environmental factors and human disease. It has always been extremely difficult, if not impossible, to establish causal relationships between environmental insults and adverse health consequences when the two are separated by long latency periods. Thus, the relation between environment and disease remains, to a significant extent, an explored but unproven assumption.

The Task Force has been aware of and sensitive to these facts. During the early part of FY82, the Task Force reviewed its past activities to assess accomplishments and chart new directions. The Task Force is in the process of reviewing what is known about the link between environment and disease and will then determine what information is missing. Research recommendations will be formulated on the basis of the identified gaps in knowledge.

The Task Force decided to focus, first of all, on the implementation of Section 402(b)(1) of P.L. 95-95.* To this end, the Project Group activities were redirected as follows:

- The Project Group on Exposure and Metabolic Mechanisms established two subgroups, one on exposure and one on metabolism, to analyze in detail the research needs identified by the 1981 Workshop on Exposure to Environmental Agents, Their Metabolism, and Mechanisms of Toxicity. These groups will develop recommendations for research for consideration by the Working Group.
- The Project Group on Standardization of Measurements and Tests was discontinued; a new project group on quality assurance (QA) was established to review Agency QA programs and promote interagency cooperation in the development of analytical methodology and the maintenance of uniform standards.
- The Project Group on Education of the Public and of Health Professionals began investigating strategies for the dissemination of existing information to the public.
- The IEPLG began a pilot study to identify long-term interagency coordination and funding mechanisms for health professional educational programs.

In accordance with the recommendation in the Fourth Annual Report for study of legal impediments to epidemiology research, the Task Force determined that a quantitative study of the overall importance of this issue as it affects health research is needed. To this end, the Task Force will attempt to estimate from the ongoing studies within each of the Federal Agencies of the Task Force the number of epidemiologic studies negatively affected by current legislation and the magnitude of this effect.

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* See page 133.

In addition, the Task Force began planning a major workshop on environmentally related nononcogenic lung diseases. Such lung diseases are within the Task Force's scope of interest, but relatively sparse information exists about the relationship of lung diseases to the environment. The objective is to identify research needs and examine the plausibility of ways to meet these needs and the associated costs. The identified needs will be submitted to the Task Force Working Group and then to the Agencies for their consideration. The workshop is planned for FY83.

To promote continued coordination in Agency research planning and help avoid research gaps and unnecessary overlaps among member Agencies, the Task Force is seeking to develop a mechanism for the exchange of information on output emanating from research programs and changes in programs. One such mechanism under consideration is the facilitation of ad hoc meetings to enable persons responsible for health research planning in one Agency to meet with their counterparts in other Agencies.

These new Task Force activities that focus specifically on the legislative mandate are described in detail in Chapter 6. Ongoing Task Force efforts are also described in Chapter 6, and Appendix C contains a listing of the publications that have originated from the Task Force over its 5 years of existence.

As background to its refocusing on the scientific problems involved in addressing its mandate, the Task Force prepared brief summaries of the state of the science in assessing the link between environmental factors and human cancer, heart disease, and lung disease. These overviews, presented in Chapter 3, are oriented to the human disease experience: reported adverse effects, believed to be associated with human exposure to environmental pollutants, are summarized. This information is presented as part of the first step in a process intended to identify gaps in knowledge and needs in environmental disease research, and should not be considered comprehensive or definitive.

Environmental disease prevention, another aspect of the Task Force's mandate, is introduced in Chapter 4. Chapter 5 presents descriptions of each member Agency's research in environment-related disease, recent research findings, and relative research priorities. This information was provided by the Agencies' Directors.

In 1982, the Task Force is actively pursuing exploratory forays to ensure the detailed and thorough assessment of the state of the science that is a necessary prerequisite to the recommendation of a comprehensive research program for consideration by the member Agencies. It is hoped that this assessment will be used to suggest directions of future research activities that will enable the determination of the relationship between environmental pollution and human cancer and heart and lung disease.

Chapter 2

RECOMMENDATIONS TO CONGRESS

To emphasize and highlight important areas of environmental health research, the Task Force formulates recommendations for transmittal to Congress. The Task Force represents those Agencies most directly involved in the area of environmental health and hopes that Congress will consider its recommendations in deliberations relevant to the health of our people and the environment.

FIFTH ANNUAL REPORT RECOMMENDATIONS

> RECOMMENDATION 1: Now that the National Death Index is operational and beginning to be of benefit to the health and medical research community, it is important that a high priority be given to its continued operation under the auspices of the National Center for Health Statistics.

The National Death Index (NDI) is a central, computerized index of death record information compiled from magnetic tapes submitted under contractual arrangements to NCHS by State vital statistics offices. These tapes (beginning with deaths occurring in 1979) contain a standard set of identifying data for each decedent. The data are used in searches of the NDI to identify and locate death records filed in the State offices. The NDI enables investigators conducting statistical studies to determine if persons in their studies may have died; if so, the Index provides the names of the States where the deaths occurred, the corresponding death certificate numbers, and the dates of death. The NDI user can then make the necessary arrangements with the appropriate State offices to procure copies of death certificates or specific statistical information such as cause of death.

The NDI currently facilitates prospective studies in medical and health research; however, as more years of death are added to the file, this new service also will be of tremendous benefit to retrospective studies. Investigators have expressed great enthusiasm for the establishment and continued operation of the NDI program because it reduces the time, expense, and effort involved in State file searches. In the past, investigators conducting both prospective and retrospective studies have often found it necessary to contact all or most State vital statistics offices, asking each to search its files to see if a death record may have been filed for any individual in the entire study group. Such studies frequently include thousands of subjects and cover long periods of time because the case fatality rates may be small and because the latent period between exposure and onset of disease may be long. Furthermore, State vital statistics offices cannot always promptly undertake large file searches because of staff limitations.

NCHS will provide the NDI user with an indication that a particular individual in the user's file has been involved in a possible match with one or more records in the NDI file. It is the user's responsibility to (a) assess the quality of each possible NDI record match that occurs, (b) determine which of the NDI records appears most likely to be associated with the person under investigation when there is more than one possible match, and (c) obtain copies of relevant death certificates or specific death-record information from the appropriate State vital statistics offices.

Death registration is a State responsibility; death certificates are filed in the States in which the deaths occur. Each State vital statistics office retains the authority to furnish NDI users with copies of death certificates or statistical data from death certificates in accordance with its legislation, regulations, and policies.

Beginning with deaths occurring in 1979, the NDI file contains death record information for all 50 States, the District of Columbia, Puerto Rico, and the Virgin Islands. The data base management system in which the data are stored is updated annually. Approximately 2 million death records are added to the NDI file each year. All State data for a given calendar year are expected to be received, processed, and added to the national file approximately 12 to 15 months after the end of the calendar year. Death records for 1979 and 1980 are currently available for searches. Records for 1981 should be available in the first quarter of 1983.

Investigators interested in using the NDI are encouraged to make every effort to collect as many of the NDI data items as possible. The following group of data items is most important because various combinations of these items are used for searching the NDI file to determine possible matches: first and last name, father's surname, social security number, and month and year of birth. As a minimum, each request must include the person's first and last name and either the person's social security number or month and year of birth. A second group of data items is used to assist the investigator in assessing the quality of possible matches that occur: middle initial, day of birth, state of birth, state of residence, sex, race, marital status, and age at death (actual or estimated).

The NDI may only be used for statistical purposes in medical and health research. In order to use the NDI, an investigator must submit a completed application form to NCHS. After being notified that the request has been approved, the investigator then prepares and submits the names (and related data) to be used for a search of the NDI file. Fees for this service consist of a basic service charge of $100 plus a 10 cents per record charge for each record submitted to NCHS on magnetic tape.

Copies of the NDI User's Manual and application form have been mailed to over 1,000 potential NDI users since November 1981, and NCHS is beginning to receive and process requests from users. The number of NDI users is expected to increase significantly in the future as more years of data are added to the NDI file and as more investigators become aware of this new service.

The User's Manual explains how the NDI functions, the restrictions on the use of the NDI, how applications for use of the service are submitted to NCHS, how lists of individuals are submitted for searches of the NDI file, the results users can expect to receive, and NCHS charges for NDI services. To receive copies of the manual and application form contact:

National Death Index
Division of Vital Statistics
National Center for Health Statistics
Room 1-44, Center Building
3700 East-West Highway
Hyattsville, Maryland 20782

RECOMMENDATION 2: It is important to develop effective procedures to minimize or remove legal impediments to epidemiologic research at both the Federal and non-Federal levels.

Although the Task Force's Fourth Annual Report to Congress contained a recommendation on this issue, the problem still exists. To conduct meaningful studies of disease occurrence and distribution in the population, epidemiologic researchers must be able to obtain data on individuals. Often there is a need for long-term follow-up of identified individuals, especially in studies of chronic disease. Epidemiologists and other medical research workers need access to various types of records, files, and data tapes often at repeated intervals to measure increases or decreases in disease prevalence. Procedures now available can be provided for safeguarding the confidentiality of the data and for maintaining the individual's right to privacy.

Federal Agencies with essential records include the Social Security Administration, the Internal Revenue Service, the Health Care Financing Administration, the Department of Defense, the Veterans Administration, and the Census Bureau. Procedures can and should be developed for providing access to records for approved medical research purposes. Protection of individual privacy could be guaranteed by agreement between the Agency and the researcher.

A mechanism should be developed in the non-Federal sector--hospitals, labor unions, and industry, which have essential confidential records--to provide approved access by epidemiologists and other medical research workers. The organization and the researcher would agree to maintain the confidentiality and privacy of the data, which would only be used in the conduct of epidemiologic research.

RECOMMENDATION 3: Professional medical organizations and Federal agencies with interests in environmental health should be encouraged to coordinate their efforts toward establishing joint initiatives to promote the education of medical and other health care students and practitioners in environmental disease prevention.

The prevention focus provides a conceptual approach that integrates scientific knowledge with health promotion. Efforts to inform health professionals, using a prevention focus, must take into consideration current clinical knowledge, attitudes, and medical practices. The "prevention focus" is an inclusive term, which can be subdivided into the following three categories:

- The identification and control by appropriate interventions of those environmental factors that influence the occurrence of cancer, heart disease, and lung disease.
- The identification and modification by appropriate interventions of symptoms that suggest a high probability of the impending onset of diseases.
- The identification and modification by appropriate intervention of psychological, social, economic, and physical sequelae that are often associated with the diagnosis, treatment, rehabilitation and continuing care of patients with cancer, heart disease, and lung disease.

The emphasis, however, for control of environment-related disease will be placed on the identification and control of environmental factors that influence the occurrence of cancer, heart disease, and lung disease. The type of prevention that should or could be implemented is determined by what is currently known about preventing specific types of cancer and heart and lung disease that are environmentally related and what relevant medical practices are available.

Physicians and other health professionals need to be aware of the influence of environmental and workplace factors on general public health. Education of physicians and other health care professionals should include consideration of environmental and workplace factors within the context of the prevention focus.

Chapter 3

ENVIRONMENTAL FACTORS RELATED TO CANCER, HEART DISEASE, AND LUNG DISEASE

The first of the Task Force's mandates is to recommend a comprehensive research program to determine and quantify the relationship between environmental pollution and human cancer and heart and lung disease. The Task Force recognizes the scientific complexities involved in implementation of this mandate and, as a preliminary information-gathering step, has prepared brief summaries of existing information on the relationship of the environment to the three diseases of concern. These summaries are overviews of some of the relevant literature and should not be considered definitive or comprehensive.

The first section of this chapter discusses pollutants in water and air in relation to human cancer, the second section deals with environmental factors related to heart disease, and the third section reviews the effects of environmental pollutants on the respiratory system. These summaries were contributed by the DHHS Task Force Agencies whose missions include research on cancer and heart and lung disease.

CANCER

It has been difficult to assess the role of environmental factors in causing human cancer because humans are exposed to multiple stresses of both physical (e.g., radiation) and chemical agents. The chemical agents may include a spectrum of chemical classes that impose cytotoxic effects on the host and possess carcinogenic, cocarcinogenic, mutagenic, or teratogenic activities (Kraybill and Mehlman 1977). Within the carcinogenic and mutagenic categories are those agents that may act through genotoxic or epigenetic mechanisms, and the modes of action of such chemicals may be important in assessing their potential hazards.

Many of these chemicals, both naturally occurring and manmade, contaminate the water, air, soil, and food-chain. In addition to exposure to these general pollutants, individuals may receive additional exposures at work to chemical or physical agents. Therefore, individuals may be subject to multiple exposures to general pollutants that, combined with personal lifestyle factors (e.g., tobacco, alcohol, diet), may result in a synergistic or additive effect in terms of cancer risk. (See section of this chapter on Air Pollutants and Lung Cancer.)

The exploitation of natural resources has resulted in the identification of many environmental stress agents, including both organic and inorganic compounds. In addition, industrial technology introduces approximately 1000 chemicals each year, and these compounds are found in a host of consumer and industrial products. However, only a small fraction (approximately 30) of the many chemicals tested have been shown to cause cancer in humans (Doll and Peto 1981). In this regard, only a limited number of these chemicals have been or are likely to be evaluated through epidemiological studies.

Carcinogenic insults to humans and animals may come from chemical, physical, or biological agents (e.g., tumor viruses), which increase the probability of tumor formation. Such toxic materials have been shown to be a hazard to humans through laboratory experiments and epidemiological studies. In animal studies, carcinogenic agents may cause an increase in the number of rodents bearing tumors, an increase in the number of tumors per rodent, or a reduction in the latency period for induction of tumors.

The identification of human carcinogens has usually been possible in special groups of individuals who have had a known elevated exposure to agents that are not present to any appreciable extent in the general environment. The difficulties in establishing exposure to a given agent(s), and the long latent period required for the development and expression of neoplasia make the problem of identifying environmental carcinogens in nonoccupationally exposed groups difficult.

Early estimates suggested that the majority of all human cancers were caused by environmental agents (Boyland 1969; Higginson 1969), but more recent analyses indicate that environmental pollutants other than cigarette smoke, may be etiological factors in only a very small percent of all cancer deaths (Doll and Peto 1981). The Doll and Peto analysis does imply, however, that 20,000 deaths in the United States each year are potentially preventable through the control of workplace exposures to carcinogens. The area of occupational cancer estimates has been controversial and is under study by the Public Health Service.

Although definitive evidence is currently lacking to establish the link between general environmental pollutants and human cancer, there are many areas of concern that require further study. For the purpose of illustration, the following subsections describe the state of the science regarding the role of environmental pollutants in water and air as possible etiologic agents in human cancer.

Drinking Water as a Source of Environmental Contaminants

Humans are exposed to environmental contaminants in their drinking water. The contaminants may occur naturally or may be added by industrial effluents, municipal effluents, or agricultural chemicals that result in runoff into streams, lakes, and rivers. The magnitude of the problem of groundwater contamination by certain organic solvents and pesticides is just beginning to be realized, and probably no water resource is free of contaminants. Classes of water contaminants include microorganisms, particulate matter, inorganic solutes, organic solutes, and radionuclides (NAS 1977).

Before the institution of modern drinking water treatment (coagulation, sedimentation, filtration, and disinfection), pathogenic microorganisms in water were an important cause of gastroenteric disease (Kraybill 1980a). Although water treatment has greatly reduced the incidence of such diseases, waterborne diseases are still of concern in the United States. According to the Safe Drinking Water Committee of the National Academy of Sciences in 1975, more than 10,000 cases of waterborne enteric diseases were reported, but for only 10 percent of these cases were causal agents identified. Some of these disease outbreaks are attributable to treatment deficiencies or problems in the distribution system.

Chlorine is the standard disinfectant agent used in most municipalities, with ozone used in some cases. While chlorine is not an ideal disinfectant and other agents have been proposed, much more exploratory work will have to be done before a satisfactory substitute is found.

Chlorination introduces a spectrum of molecular species hitherto unidentified in the raw water supplies from which the municipal drinking water is derived (Helmes et al. 1981).

When coagulation and filtration are not applied, suspended particles may indirectly reduce the efficiency of the disinfection process and serve as carriers of other contaminants in the drinking water. Asbestos and asbestiform particulates, for example, could have a direct effect on human health (Mason, McKay, and Miller 1974). Lake Superior, which is a resource for drinking water in Duluth, Minnesota, and surrounding communities, is heavily contaminated with taconite tailings containing mostly amphiboles (Mason, McKay, and Miller 1974). Studies using experimental animals have been undertaken to ascertain the role of ingested particles, such as asbestos minerals. The National Toxicology Program (NTP) conducted feeding studies of several types of asbestos minerals using hamsters. The results showed no significant treatment-related increase in the incidence of tumors in these animals.*

While there is a wide array of inorganic solutes in water, only 22 have been reviewed extensively for potential health effects. Of this group of 22 inorganic cations and anions, 13 are trace metals or essential nutrients (Sharrett 1979). High levels of these metals may be toxic, but none have been shown to be causes of serious health problems at the levels that are normally present in water. The metal having a great potential for toxicity is lead. Setting standards for lead involves consideration of all sources of intake, including air and diet. The Maximum Contaminant Level (MCL) for lead in drinking water is 50 parts per billion. Current thinking is that the present water standard for lead may not provide an adequate margin of safety, especially for infants and children (Masironi 1978; NAS 1977).

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* Current policy is that all draft NTP Technical Reports of Carcinogenesis Bioassays are peer reviewed at an open public meeting by the Review Subcommittee of the NTP Board of Scientific Counselors. The review of the draft asbestos hamster feeding studies took place in June 1981 at NIEHS, Research Triangle Park. The published reports include the comments of the Review Subcommittee, where applicable. This particular report is not published yet.

Radioactivity in water, in particular uranium, radon, potassium-40, manganese-55, strontium-90, cesium-137, cerium-144, and radium-226, has been investigated because the alpha and beta activity of these radionuclides may induce cancer, specifically bone cancer from radium-226, radium-228, and strontium-90 (NAS 1972). Flocculation and water softening may help in the removal of radium from water (Hickey and Campbell 1968).

Some radioactivity in drinking water comes from fallout, but most is the result of groundwater passing through geologic deposits of radiochemical materials (NCRP 1975). Inadvertent disposal of radioisotopes or radio-pharmaceuticals into water supplies can also add to the total environmental levels. It is estimated that the radioactivity contained in water is only a small fraction of the total normal background radiation to which all people are exposed (Lucas 1971). For this reason, the risk of adverse health effects (mutagenic, carcinogenic, or teratogenic) attributable just to waterborne radioactivity is difficult to establish, but is likely to be low for the majority of the population. However, in some water supplies, radium reaches concentrations that may pose a risk of cancer (Rowland, Lucas, and Stehney 1977). Consequently, each major water supply should be surveyed to determine whether radioactivity is present and to what degree. Monitoring for radium and other natural radionuclides in drinking water from ground sources is required at 3-year intervals. The MCL for radium-226 and radium-228 is 5 picocuries per liter. The MCL for gross alpha particle activity is 15 picocuries per liter.

Of the wide spectrum of detected organic water contaminants that have been tested in the appropriate experimental systems, 20 have been categorized as recognized carcinogens, 24 as suspected carcinogens, 50 are considered mutagens, and 18 are thought of as promoters or cocarcinogens (Helmes et al. 1981). Some in vitro and in vivo experimental studies have identified some carcinogenic and mutagenic activity in contaminated water (Helmes et al. 1981). Few of the identified contaminants have been bioassayed for carcinogenesis or mutagenesis.

There have been numerous epidemiological studies conducted on populations living in various river basins. Factors considered in these studies include the effects of groundwater and surface water, chlorinated versus nonchlorinated water, and the presence of trihalomethanes to indicate contamination. Some of the epidemiological studies have suggested statistical associations between such factors and cancer incidence (Kraybill 1980a). The interpretation of these epidemiological studies, however, is limited because of uncontrolled variables, and future studies should attempt to correct these deficiencies. While the experimental and epidemiological studies may provide some presumptive evidence and insights of causal associations between the occurrence of cancer and exposure to micropollutants (parts per billion and parts per trillion levels of occurrence), no firm conclusions are yet possible.

More sophisticated experimental studies are planned by NCI and EPA using various animal models and in vitro systems. These studies may provide a better understanding of human risk from exposure to environmental contaminants (Kraybill 1980b). There is indeed concern, however, that ingested carcinogenic and mutagenic contaminants may contribute to the total cancer burden.

The Role of Air Pollutants in Causation of Human Lung Cancer

With the increase in industrialization during the last three decades, cancer mortality has been associated with residence in industrialized urban areas (Ford and Bialik 1980). However, the evidence pointing to ambient air pollutants in these areas as the sole etiologic agents is lacking because humans are exposed to a multitude of environmental pollutants from various sources (Hammond and Selikoff 1969; Doll and Peto 1981). Cigarette smoking is considered the biggest risk factor for lung cancer in the general public (U.S. Surgeon General 1982; Doll 1978).

Exposure to more than one source of air pollution may increase the risk for smokers because of the synergism between various carcinogens in the workplace and the components of tobacco smoke. Evidence now available from epidemiological studies appears to suggest that there is an increase in lung cancer in cigarette smokers who were occupationally exposed to asbestos and radon (Doll 1978). A recent review by Fraumeni (1982) states that the carcinogenic effects of radon and asbestos are greatly enhanced by cigarette smoking, and reduction of occupational exposure and/or smoking would tend to reduce the cancer risk.

In the workplace, exposure to nickel, chromates, radioactive ore, and gas-working operations has been associated with lung cancer (Kotin 1956; NAS 1980, p. 173). Other occupational causes of lung cancer include inorganic arsenic (mining and smelting), bis(chloromethyl)ether (manufacture of ion-exchange resins), and mustard gas (manufacturing) (Fraumeni 1982).

However, there appears to be little evidence showing that ambient air pollutants induce lung cancer in the general public because the lung cancer mortality of nonsmokers is extremely low, irrespective of their place of residence (Doll and Peto 1981). Cigarette smoke may interact with some air pollutants to increase the incidence of cancer above levels that would be expected from smoking alone (Hammond and Garfinkel 1980), but this supposition remains unproven.

Doll and Peto (1981) have estimated that tobacco may be responsible for 25 to 40 percent of all cancer deaths, whereas they estimate that air pollutants may account for less than 1 percent of all cancer deaths and no more than 1 percent of lung cancer deaths. However, other investigators have suggested that the contribution of air pollution to lung cancer may be larger than previous estimates (Wilson et al. 1980; Karch and Schneiderman 1981).

Studies of air pollution carcinogenesis are complicated because of difficulties in quantifying the exact amount of air pollutants that are deposited in the lower respiratory passages (Wynder and Hammond 1962).

Few studies have used personal rather than fixed monitors of the ambient environment to determine individual exposures to air pollutants. In addition, epidemiological studies encounter problems in defining urban and rural effects (Ford and Bialik 1980). For example, a large proportion of the American population works some distance away from their homes and experience different types of pollution in their homes, on the way to and from work, and in the workplace. Also, the American population is quite mobile, and many people move every few years (Hammond and Garfinkel 1980).

Recently, there has been increasing concern about indoor air pollution, and measurement of indoor air pollutants is just beginning to be assessed (Council on Environmental Quality 1980; NAS 1981a). Changes in insulating and heating homes in response to rising energy costs have created a new set of problems. Pollutants, such as nitrogen dioxide and carbon monoxide, are emitted from gas stoves and unvented space heaters; formaldehyde is used in foam insulation, furniture, carpets, drapes, and other household items; and radon gas is released from building materials, such as concrete or brick. The hazards of tobacco smoke and respirable suspended particulates in indoor air have been documented (NAS 1981b), and the use of woodburning stoves contributes to both indoor and outdoor pollution (Cooper and Malek 1982).

Pollutants, which can be found in outdoor air and which have been shown to be carcinogenic at certain concentrations, encompass not only the frequently cited polycyclic aromatic hydrocarbons but also nitriles, aromatic amines, halogenated aliphatics, monocyclic aromatics, N-heterocyclics, N-nitrosamines, and vinyl halides (Kelsey et al. 1982). Woodburning stoves and fireplaces are currently being investigated as sources of indoor air pollutants (Peters 1982; Cooke, Allen, and Hull 1982; Muhlbaier 1982).

Some carcinogenic air pollutants are produced from incomplete combustion processes. Cyclopenteno[cd]pyrene is a polycyclic aromatic hydrocarbon that has been shown to be a skin carcinogen in mice (Cavalieri et al. 1981). It occurs in automobile exhaust at a level 10 times that of benzo(a)pyrene, which is sometimes used as an index of air pollution in epidemiological studies (Fraumeni 1982).

Because of the rapid increase in fuel prices, people are driving more fuel-efficient vehicles, such as those having diesel-powered engines. By the year 1990, about 25 percent or more of the "light-duty" vehicles on the road may be powered by diesel engines (Rosenkranz 1982; NAS 1981c). The increased use of diesel fuel may result in increased levels of particulate emissions (Rosenkranz 1982).

New health risks may develop from diesel emissions because they contain higher levels of particulates and nitrogen oxides than exhaust from comparably powered gasoline engines (Cuddihy et al. 1981). However, epidemiological studies of occupational exposure to diesel engine emissions have not demonstrated convincingly an excess risk of lung cancer or cancer of any other site (NAS 1981d, pp. 93-96). Air concentrations of both diesel exhaust particulates and nitrogen dioxide at congested urban sites now account for 30 to 50 percent of the current levels of pollutants in the large metropolitan areas and will likely increase in the future. Diesel effluents also contain nitroarenes, a class of compounds that is currently being studied in various short-term assays (Huisingh 1981; Ohgaki et al. 1982; Pitts et al. 1982; Li and Royer 1982). Although diesel particulates containing these and other compounds are respirable and can penetrate into deep regions of the respiratory system, no human health effects have been documented to date (Vostal 1980; NAS 1981d, pp. 121-38).

Research to link environmental factors as a cause of human cancer requires better data on the actual exposure of humans to specific environmental pollutants in various biological media. Such exposure data are extremely important to the successful conduct of epidemiology studies that attempt to delineate etiologic agents of cancer and other diseases in individuals who are exposed to a multitude of environmental pollutants (Task Force on Environmental Cancer and Heart and Lung Disease 1981). However, because of the extreme lag between exposure and onset of disease, establishing cause-and-effect relationships by such epidemiology studies requires that population groups that experience elevated or consistent levels of exposure to specific environmental pollutants be tracked and monitored over a long period of time.

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HEART DISEASE

A number of reviews pertaining to the importance of environmental factors in diseases of the heart have been published. A recent report, one of the more comprehensive documents, was produced by an ad hoc task force formed by the American Heart Association and published in the journal Circulation (Harlan et al. 1980).* The group was asked to examine the available scientific evidence, to identify areas where the data indicated important environmental risk and to note promising lines of inquiry. Relevant sections of the introduction and summary are cited below:

> The public and health professionals share an increasing concern that the environment may play an important role in development of disease. Recognition that natural and manmade environmental factors initiate or facilitate tumor development has prompted questions about environmental influences on the pathogenesis of other diseases, particularly cardiovascular disease, and the extent to which harmful influences may be altered or controlled. It is generally recognized that demographic, social, and psychological factors can influence development of rheumatic, hypertensive, cerebrovascular, and ischemic heart disease. Many of these factors are under personal control, but some are features of the general environment. Particular public concern has been directed to features of the environment, such as toxins encountered in occupational settings or in general living situations that might be identified and regulated. Legitimate concerns are being expressed about exposure to chemicals, dusts, and natural toxins that are ubiquitous in the environment but potentially harmful....
>
> Broadly considered, environmental hazards comprise both features of the ambient environment and aspects of environment that are personally controlled. Examples of ambient hazards are contaminants in air, water, and food that

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* Harlan, W.R. (Chairman), Sharrett, A.R., Weil, H, Turino, G.M., Borhani, N.O., and Resnekov, L., of the American Heart Association Task Force on Environment and the Cardiovascular System. Circulation 63:242A-271A 1980.

result from natural variations or from actions taken by manufacturers and processors. In addition, occupational hazards represent potential risks that cannot be controlled by the worker, but to which he or she is, nevertheless, exposed. Large numbers of people may be exposed to general environmental hazards and individuals usually cannot identify, avoid, or modify these environmental features. Public action and regulation is usually necessary.

On the other hand, certain aspects of environment are under control. These include food selection, cigarette smoking, various drugs, and a variety of health habits such as physical activity. Advice and education is the appropriate intervention for personal hazards.... Personal environmental factors are important risk factors in the development of cardiovascular disease and, based on present knowledge, appear to make greater contributions to disease development and progression than do general environmental factors....

...these distinctions may be blurred somewhat in the area of diet. Personal selection may determine the types of foods purchased, but some aspects of food choice may not be controlled by the consumer. Practices in growing food, raising livestock, and in the processing of foods are not under individual control but can make important nutritional contributions. The pervasive use of salt in food processing and preparation of convenience foods is an example....

Potential environmental hazards were separated by categories of exposure and some of the conclusions are summarized below:

Water Hardness

There are differences in the prevalence of cardiovascular disease, particularly coronary artery disease and hypertension, that appear to be related to geographic region. These differential rates have been attributed to differences in water hardness among regions. However, when examined closely, the associations between water hardness and mortality rates have been weak and inconsistent and the relationships to individual water constituents have also been inconsistent. Based on present evidence, no firm conclusions can be drawn regarding the relationship between water hardness and cardiovascular disease, and no public health action seems necessary now. Future research should focus on individual constituents of water, particularly magnesium, and should include investigation of their biologic effects. There are other sources of human intake of these biologically important constituents and their contribution should be assessed.

Trace Elements

These elements are ubiquitous, electropositive elements essential for life, although present in the human body in small quantities. They are critical to the action and control of many enzymes and are derived from many sources, including industrial processes. Scattered reports indicate that excesses or deficiencies may be associated with cardiovascular damage or alteration in other risk factors. Several current studies, both national and a collaborative international investigation, are directed toward a more comprehensive examination of the clinical and pathological effects of trace elements. There is insufficient evidence on which to base a definitive statement. In general population studies, the associations lack consistency or rigorous scientific backing. Further study, including investigation of basic biologic action of these elements, is needed.

Inhalant Occupational Exposure

Several inhalant exposures, primarily from industrial sources, have been proposed as toxic to the cardiovascular system. Only with respect to workers exposed to carbon disulfide and explosives is the association established. While the potential of other occupational exposures has been suggested, the capability of directly producing heart disease is considered to be tentative. However, such exposures may have an indirect effect by influencing risk factors for cardiovascular disease.

Occupational cohorts afford a valuable opportunity for investigation of environmental hazards because the intensity and duration of exposure can be measured and many health parameters are being assessed currently. The role of occupation as a risk factor in cardiovascular mortality and morbidity deserves further study.

Carbon Monoxide

Carbon monoxide is a product of natural and manmade chemical processes and, in excess, can have important biological effects, including profound effects on the cardiorespiratory system. The function of the cardiovascular system can be compromised by carbon monoxide primarily because of decreased oxygen-carrying capacity of the blood. This compromise in cardiovascular function is most notable in individuals with underlying vascular disease, but is demonstrable in normal individuals at levels of 18-20 percent carboxyhemoglobin. There are numerous environmental sources and particular occupational groups may receive even greater exposures, but it should be emphasized that the personal habit of smoking remains the greatest potential source of carbon monoxide for the general population. Considerably more basic investigation of the effect of carbon monoxide on vascular reactivity, atherogenesis, and myocardial irritability and dynamics are required before recommendations can be made regarding "safe" levels of carbon monoxide exposure.

Noise...

Noise exposures at levels of 90 dBA and above are relatively common in our industrialized society. At such levels, noise may initiate cardiovascular responses that mimic an acute stress effect. Blood pressure inceases, changes in blood hormones and biochemistries have been reported to occur in industrial settings and have been attributed to noise exposure. However, the reported changes are not consistently found by all investigators and the observations have been confounded by inadequate control of other variables and conflicting results....

Some common conclusions emerge from review of the environmental impact on the cardiovascular system. First, it is worthwhile to reiterate that personally controlled environment--cigarette smoking, diet, obesity--is more important in the pathogenesis of cardiovascular disease than the general or ambient environment. However, the pervasive nature of the environment means that even a relatively minor influence on cardiovascular health can have impact on major segments of the population. There is a clear need for further investigation. In this regard, the lack of evidence for profound effects of the ambient environment may reflect the lack of research directed to this problem, as well as the apparent absence of major effects.

LUNG DISEASE

This section will review the involvement of the environment in the occurrence of respiratory diseases other than lung cancer.

The respiratory system is the one system of the body, other than the skin, that is constantly exposed to the outside environment. Because air pollution has long been suspected to play a role in lung disease, considerable effort has been directed at this relationship with results that frequently have been inconclusive. Nonetheless, there continues to exist a growing body of information that implicates the environment in the development of pulmonary disease or, more commonly, the exacerbation or aggravation of preexisting or predisposing conditions.

Several studies indicate that when smoking is excluded as a factor, there appears to be little evidence of a health effect on asthma patients from outdoor air pollution with the exception of sulfur dioxide. Other factors, such as allergens, appear to have a greater effect in the pathogenesis of asthma, together with indoor pollution from smoking and nitrogen dioxide from gas stoves. Indeed, cigarette smoke appears to be the most critical air pollutant (Bouhuys and Gee 1980). Pollution in the form of dust from grain elevators and combustion particles from burning dumps has been suggested as a possible cause of asthma epidemics in New Orleans. These became evident when hospital emergency rooms showed sharp increases in visits from patients with asthma attacks at certain times of the year (Higgins 1974, p. 46).

Studies of effects of environmental pollutants have usually depended on measurements of pulmonary function and on symptoms such as cough, wheezing, shortness of breath, and irritation of mucous membranes.

It is often difficult to distinguish chronic bronchitis from emphysema by means of these symptoms alone. Cigarette smoking is implicated strongly in emphysema (NHLBI 1981) as in chronic bronchitis. Most studies on chronic bronchitis also note the coexistence of emphysema. In England and Wales, high positive correlations were noted between Standardized Mortality Ratios (SMRs) for bronchitis and atmospheric deposits (total suspended particulates) and atmospheric smoke (Stocks 1959). In another study, it was found that high levels of pollution increased the frequency of bronchitis, and this effect was most marked for cigarette smokers (Lambert and Reid 1970).

That air pollution can be fatal has been reported for over a century. The British Ministry of Health has recorded lethal fog in London as far back as 1873. These deaths and those in subsequent London fogs were most often attributed to bronchitis, but also to heart disease and to other respiratory diseases (NAS 1977). Studies of episodes of high pollution levels in New York City also showed increased mortality, and during periods of sustained high pollution levels, morbidity as well as mortality rates increased in both cities. In London and in New York City, excess deaths occurred when sulfur dioxide was high (NAS 1977).

Three independent longitudinal studies of lung function and mortality and morbidity in London show interesting trends and correlations. One such study in 1960 showed significant correlations between pollution and diseases during the early years of the study, but little evidence of any effect of pollution on mortality or morbidity was found in later years (NAS 1977, p. 247). This has been attributed to the sharp decrease in that city's pollution since 1958. Similarly, when 1,000 chest clinic patients with chronic bronchitis and emphysema were examined during the winter of

1959-60 in London, there were high positive correlations between symptoms and concentrations of smoke and sulfur dioxide (NAS 1977, p. 251). When the observations were repeated 5 years and 7 years later after smoke concentrations in that city had declined considerably, successively lower incidence of disease was seen. A third study revealed that respiratory illnesses in a regularly observed sample of over 1,000 men living in London varied with the concentrations of smoke and sulfur dioxide in the districts where the men lived (NAS 1977, p. 250).

Two studies in Chicago also related environmental factors with symptoms in patients with bronchitis. An increase was observed in the frequency of respiratory illness in men aged 55 and older who had severe chronic bronchitis, and this increase correlated with increases in sulfur dioxide in the environment (Carnow et al. 1970). In contrast, younger men and women showed no relation between sulfur dioxide concentrations and frequency of respiratory illness.

Studies of children are important because they are not subject to occupational exposures, and cigarette smoking is a less likely factor to be considered than among adults. In addition, children may be more sensitive to air pollution than adults. It has been suggested that bronchitis may begin in infants or children as a possible effect of pollution and shown that mortality from bronchitis at young ages exhibits international patterns (NAS 1977, p. 268). The medical following of school children in Sheffield, England, revealed a progressive increase in respiratory illness from lowest to highest air pollution concentrations (NAS 1977, p. 269). In another study of children, lower respiratory infections were consistently related to pollution, but upper respiratory infections were not (NAS 1977, p. 269). Also, both the severity and frequency of these infections increased with the amount of pollution.

Reducing air pollution can apparently reduce the prevalence of respiratory disease and improve lung function. A followup study conducted in Berlin, New Hampshire, 6 years after the original study demonstrated that after allowances were made for aging and cigarette smoking, there was a decline in the prevalence of chronic respiratory disease and a slight improvement in lung function measurements (NAS 1977, p. 276). Both sulfation rates and total suspended particulate concentrations had decreased during the 6-year period between the original study and the followup. The comparison of the two notorious London fogs of 1952 and 1962 revealed similarly that there were an estimated 4,000 excess deaths associated with the 1952 episode, while only 700 were associated with the 1962 episode (NIAID 1979). This difference was attributed to the marked decrease in the particulate emission level of 1962.

The problem of environmental lung disease is one of assessing the effects on the lung of relatively low doses of agents. Occupational lung diseases are a different category of "environmental" insofar as they generally entail large doses, or at least doses significantly above those found in the general community environment. These diseases, including silicosis, asbestosis, farmer's lung disease, byssinosis, and coal worker's pneumoconiosis, to name but a few, have been and continue to be studied vigorously. They are not included here because of their specialized "environmental" nature. They should, nonetheless, be kept in mind when one thinks of environmental lung disease because it is likely that research findings on these diseases may be relevant to the study of diseases related to the general environmental pollution.

In order to better delineate the problems of nononcogenic lung disease, a workshop is presently being planned by the Task Force. It is hoped that the workshop will provide an up-to-date synthesis of what is known about environmental lung disease, as well as recommendations for future research directions to lead us to solutions to the problem of environmental pollution as it affects the lung.

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Chapter 4

PREVENTION OF DISEASE

The study of disease logically extends to the study of disease prevention. This was recognized by Congress when it directed the Task Force to "recommend research and such other measures as may be appropriate to prevent or reduce the incidence of environmentally related cancer and heart and lung diseases" (P.L. 95-95, Sec. 402(b)(3)). Task Force consideration of disease prevention coincides with an important Federal policy emphasis on prevention.

Health promotion and disease prevention constitute one of the major strategies of the Department of Health and Human Services (HHS). The development of the national prevention strategy began in the early 1970's with the President's Committee on Health Education (1971), followed by the Preventive Medicine Task Force of the Fogarty Center and the American College of Preventive Medicine (1975), the Department of Health, Education, and Welfare's (HEW) Task Force on Disease Prevention and Health Promotion (1978), the Surgeon General's Report on Health Promotion and Disease Prevention, Healthy People (1979), and Promoting Health/Preventing Disease: Objectives for the Nation (1980).

This last document sets a series of over 200 specific, measurable objectives for the year 1990 covering 15 priority areas that are the key to achieving national health aspirations. Two of these areas include objectives relevant to the Task Force on Environmental Cancer and Heart and Lung Disease--toxic agent control and occupational safety and health. The other 13 priority areas are high blood pressure control, family planning, pregnancy and infant health, immunization, sexually transmitted diseases, accident prevention and injury control, fluoridation and dental health, surveillance and control of infectious diseases, misuse of alcohol and drugs, smoking and health, nutrition, physical fitness and exercise, and control of stress and violent behavior.

The objectives within each priority area address five types of health promotion activities: improved health status, reduced risk factors, improved public/professional awareness, improved services/protection, and improved surveillance/evaluation. The following are examples of objectives most related to activities of the Task Force in the priority areas of toxic agent control and occupational safety and health.

Toxic Agent Control

Several objectives deal with increased public/professional awareness, e.g.:

- By 1990, at least half of all people ages 15 years and older should be able to identify the major categories of environmental threats to health and note some of the health consequences of those threats.

Others deal with improved services and protection, e.g.:

- By 1990, every individual residing in an area of a population density greater than 20 per square mile, or an area of particularly high risk, should be protected by an early warning system designed to detect the most serious environmental hazards posing imminent threats to health.

Occupational Safety and Health

- By 1990, at least 25 percent of workers should be able, prior to employment, to state the nature of their occupational health and safety risks and their potential consequences, as well as be informed of changes in these risks while employed.
- By 1985, workers should be routinely informed of lifestyle behaviors and health factors that interact with factors in the work environment to increase risks of occupational illness and injuries.
- By 1990, at least 70 percent of primary health care providers should routinely elicit occupational health exposures as part of patient history, and should know how to interpret the information to patients in an understandable manner.

Implementation plans for each of the 15 priority areas are now being developed and will be published as a companion document to Objectives for the Nation. Preliminary drafts of the final implementation plans have been distributed for review, but final plans have not yet been approved.

Prevention activities within the National Institutes of Health (NIH) are now coordinated by a new NIH Disease Prevention Research Program established in October 1981. One of the primary functions of this office will be to assist individual Institutes in identifying opportunities for prevention-related research and to coordinate the existing prevention activities of the Institutes.

It is within the mission of some of the member Agencies of the Task Force to develop prevention strategies, and some Agencies have primary responsibility for one or more of the 15 priority areas. NHLBI is the lead Agency for the high blood pressure control area; NIEHS for the toxic agent control area; and NIOSH for the occupational safety and health area. A broad description of prevention activities of HHS are described in Prevention '82 (to be released in the fall of 1982). A diverse group of non-HHS Federal programs in health, education, social services, nutrition, recreation, transportation safety, and environmental protection also provide opportunities for promoting health and preventing disease. Prevention '80, also by HHS, described the prevention activity of other departments and Agencies, such as EPA, the Federal Trade Commission, U.S. Department of Agriculture, Consumer Product Safety Commission, and U.S. Department of Labor.

As the Task Force develops its prevention activities, it will coordinate with other prevention-related activities and programs. The Task Force will continue to work closely with the Office of the Deputy Assistant Secretary for Health (Disease Prevention and Health Promotion) and the NIH Disease Prevention Research Program.

Chapter 5

OVERVIEW OF RESEARCH IN TASK FORCE AGENCIES

The Task Force's First Annual Report to Congress (August 7, 1978) included a summary of member Agency research programs that were related to the scope of the Task Force's effort for the first year--namely, relationships between chemical pollution and disease. For this Fifth Annual Report to Congress, each member Agency Director provided an updated overview of research studies or programs that are aimed at the relationship of environmental factors to human cancer and heart and lung disease. This chapter also includes recent research advances and findings and relative research priorities, as identified by the member Agencies.

U.S. ENVIRONMENTAL PROTECTION AGENCY

A major objective of EPA's research is to determine the risks to human health of pollutants that are discharged into the environment. Various scientific disciplines are involved in the research effort, primarily conducted by the Office of Research and Development (ORD), the Office of Pesticides and Toxic Substances (OPTS), and the Office of Air, Noise, and Radiation (OANR).

Office of Research and Development

Because modern methods of analysis enable contaminants to be measured at concentrations as low as parts per trillion, it is necessary to determine the level at which there is little or no probability of adverse health effects. The research activities of the ORD are directed toward the collection of the data necessary to qualify and to quantify the link between contaminants and potential health effects.

The Office of Health Research (OHR) within ORD performs health research in four major areas: air, water, pesticides, and toxic substances. Research in all of these areas focuses on the three objectives outlined below:

> Developing Improved Methods of Risk Assessment: The major thrust of this effort is to provide a biological basis supporting more accurate and reliable models to extrapolate data, both from animals and from high doses to low doses. EPA must rely heavily on animal test data to determine human health risks from pollutants or suspected pollutants because opportunities for human experimentation are limited. To ensure that the data obtained in all such experiments are analyzed and interpreted accurately, OHR is developing the scientific basis necessary for refining existing extrapolation models so that predictions of human risk are more reliable.
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> Assessing Dose-Response Relationships: The aim is to ascertain at what doses and under what conditions various pollutants cause measurable health effects. Animal studies, performed on normal and sensitive populations, provide a means to evaluate the effects of acute and chronic exposures. Biological endpoints of concern vary depending on the pollutants and exposure routes, but include cancer, cardiovascular, and pulmonary effects.
>
> Developing Test Methods: In this area, OHR has two main concerns. One goal is to develop and validate protocols for reliable, rapid, inexpensive bioassay techniques to identify the toxic component(s) in complex mixtures, such as mobile source emissions and newly developed synthetic compounds. Detecting potential mutagens, carcinogens, and cytotoxic agents is the primary focus of this work. OHR is also improving test methods for other endpoints, such as infectivity models, cardiovascular and cardiopulmonary disease, and biochemical responses to environmental insults. A major reason for this undertaking is to recognize subclinical signs of disease.

Research conducted at the Health Effects Research Laboratory (HERL) relating to air pollutants and lung disease has been carried out using an integrated approach in which information from epidemiology, human clinical studies, and animal toxicity is correlated. Such an approach overcomes the inherent weaknesses of any single approach and derives full benefit from their strengths.

The emphasis for the research has been on the health impact of criteria pollutants known to have pulmonary effects and of complex mixtures, which include combustion processes, such as smelter, coal-fired power plants, and automobile exhaust emissions. Current research activities, mainly in animal toxicology, include:

- Analysis of comparative dosimetric relationships between animals and man with respect to the effective dose of environmental pollutants
- Studies of the effects of common air pollutants on infectious pulmonary disease to establish effect of exposure patterns, pollutant interaction, and particle size
- Assessment of the health effects of complex pollutant mixtures on pulmonary function and host susceptibility to infection
- Investigation of susceptible subpopulation groups who may be at increased risk of health effects due to air pollution.

Studies in humans include:

- Controlled exposure of normal humans to low levels of pollutants to assess dose-response effect and effects of combinations of pollutants on various systems

- Measurements of physiological, immunological, and biochemical changes with exposure at various levels of exercise

- Questionnaire survey in young adults to determine association of pollutant concentration with symptom prevalence.

Recent advances and research findings include:

- An evaluation of the carcinogenic hazard of diesel exhaust emissions included short-term bioassay for genotoxic and carcinogenic activity. Using these data and others, the Office of Health and Environmental Assessment (OHEA) has calculated a quantitative risk estimate for human exposure to the exhaust from light-duty diesel engines.

- The long-term effects of air pollutants were demonstrated in beagle dogs exposed for 6 years to mixtures of pollutants at 2-6 times the average daily level of large cities and followed for an additional 3 years to ascertain irreversible chronic effects. Mild but unequivocal exposure-related changes in pulmonary function and structure persisted and became more pronounced after the exposure was terminated.

- Advancement of small animal pulmonary function techniques to the point that most human functional parameters can be assessed in small laboratory animals.

- Improved understanding of comparative dosimetric relationships between animals and man on the effective doses of pollutants.

- Studies of the relative role of various particles on increases in infection, showing the importance of cations.

- Studies demonstrating parallel effects in in vivo and in vitro tests served to substantiate the in vitro data.

- Combinations of sulfuric acid and carbon caused more changes in host defenses against infection than either pollutant alone.

- Exposure of normal humans to low levels of ozone results in decrements indicating disturbances in the immune system.
- The effect of nitrogen dioxide (NO_2) on infectious pulmonary disease is influenced strongly by the pattern of NO_2 exposure.
- Young rats are more susceptible than adult rats to ozone-induced changes in pulmonary function.
- A short-term inhalation exposure to Mt. St. Helens volcanic ash does not cause major immediate or delayed effects on the lungs.
- Vitamin C-deficient guinea pigs are more susceptible to the pulmonary effects of NO_2, but not ozone.
- Dose-response relationships between acute changes in lung function and symptoms and five concentrations of ozone between 0.12 and 0.40 ppm were evaluated in normal males; decrements in pulmonary function and increased symptomatology were observed at the lower ozone concentrations, levels much lower than that at which decrements have been previously reported.
- The interaction of three gases (ozone, sulfur dioxide, and nitrogen dioxide) with water soluble particles (ammonium sulfate, ammonium bisulfate, sulfuric acid, and ammonium nitrate) on lung function and immunology was studied in normal males; preliminary analyses suggest some synergism between ozone and sulfuric acid. Therefore studies in patients with chronic obstructive lung disease are being planned.
- Ozone exposure did not influence the cause of an experimentally induced upper respiratory viral infection.
- Changes in lung function were not observed in patients with mild chronic obstructive lung disease during exposure to moderate levels of ozone.

HERL has had a long-standing research effort aimed at determining the health hazard associated with pollutant materials in drinking water from U.S. cities and communities. A major area of research continues to be to define the nature of the carcinogenic potential of these contaminants.

The current research and accomplishments at HERL in environmental cancer include the development, validation, and evaluation of the short-term bioassays for the detection of carcinogens, including tumor initiators, tumor promoters, and other agents that enhance the development of cancer and thus might pose a potential human health hazard. HERL is also developing and evaluating modes for the interspecies extrapolation of animal data to humans and for the extrapolation of responses at high experimental doses to the low doses of human exposure. Research to delineate the mechanisms of action for tumor initiation and promotion are essential means to these ends.

Current research activities include:

- Development and validation of short-term bioassays for carcinogens and tumor initiators that have as their endpoint either preneoplastic lesions or tumors. An agent that is active in these assays can then be classified as either a tumor initiator or complete carcinogen.
- Improvement of short-term assays for screening substances for genotoxic activity. These assays are based on the assumed association of a somatic mutation with the initiation of cancer.
- Development and validation of bioassays for non-genotoxic carcinogens that are to be used to screen and estimate the hazard to human health of tumor promoters and other enhancers of carcinogenesis.

- Determination of the relative contribution of species differences in target organ susceptibility and of metabolism and pharmacokinetics to inter-species extrapolation procedures.

- Determination of the importance of differentiating between initiating and promoting mechanisms in chemical carcinogenesis, to the models used in risk assessment.

- The current Gene-Tox Program continues to evaluate the predictive ability of short-term genotoxic bioassays to detect chemical carcinogens.

Recent advances and research findings include:

- Evidence from epidemiologic studies of a consistent but weak association between organic contaminants in drinking water and bladder, colon, and rectal cancer. Trihalomethanes, the organic contaminants of interest, are associated with chlorination procedures.

- The initiation of carcinogenesis as measured by cell transformation in vitro or preneoplatic lesions in rat liver is associated with specific alterations in the DNA.

- The feasibility of hemoglobin binding to serve as a dose monitor for direct- and indirect-acting carcinogens has been determined in laboratory animals. The evaluation of its use in monitoring humans is underway.

- Two feasible approaches useful in providing the scientific background required for interspecies extrapolation models have been demonstrated. These include (1) the use of the comparison of human organ culture to animal target organ culture in order to determine the mechanism for target organ specificity, and (2) the impact of species variation in metabolism and activation of carcinogens.

Research efforts in relating environmental factors to heart disease have been directed at examining the influence of specific chemical constituents related to water hardness, such as calcium, magnesium, cadmium, and lead, on atherosclerotic disease and hypertension. Current studies include:

- Animal toxicity studies to delineate the interactions among chemical constituents related to water hardness and between essential and toxic trace metals
- Studies in experimental animals to develop dose-response relationships of metals found in hard and soft water
- Studies of the role of the organic chemicals and disinfectants found in water on human health
- A statewide epidemiological case-control study of the association between cardiovascular disease and drinking water quality.

Recent advances and research findings include:

- Confirmation that cadmium produces hypertension in rats and pigeons.
- Modest body burdens of lead and cadmium result in increased evidence of atherosclerotic disease in rats and pigeons.
- Cardiovascular effects of lead and cadmium are enhanced by magnesium in pigeons.
- Increased calcium intake reduces severity of atherosclerotic disease and hypertension in the pigeon.
- Magnesium antagonizes the atherosclerotic protective effect of calcium.

- Individuals in communities with high levels of sodium in the drinking water had higher blood pressures than those drinking from low sodium water supplies. However, sodium intake via food was a difficult factor to control.

OHR has identified four areas as research priorities for the future. These are:

1. Developing better ways to estimate risk--This includes all of our extrapolation work, relating biological responses to pollution with potential for disease, and data developed on structural activity relationships.

2. Researching endpoints besides cancer in air pollution programs--Cancer is not excluded as a possible consequence of air pollution exposure; rather, we are concentrating more on possible cancer precursors, such as immunological insufficiency, biochemical disorders, and genetic aberrations. Also, we have concentrated a great deal of effort on studying respiratory, cardiopulmonary, and cardiovascular effects of air pollution, using standard and newly developed technology that allows objective measurements of heart and lung performance in humans, which was previously impossible.

3. Developing better test methods--OHR is developing new screens for hazardous compounds and faster, more reliable testing methods for biological endpoints, such as immune disorders and cardiovascular disease.

4. Epidemiology--Although EPA does not conduct the long-term, prospective studies necessary, such data are useful in many areas. Since other health-related Agencies are better equipped to perform such studies and have primary responsibility for researching the biological endpoints of concern, OHR is working to strengthen EPA's cooperation with such Agencies so that environmental factors will be included as covariables in their studies. We are also making greater use of the University of Pittsburgh Center of Excellence for Epidemiology and the competitive research grants program to help meet EPA needs in this area.

Human health risk assessment performed by ORD's Office of Health and Environmental Assessment (OHEA) includes the collection, review, and analysis of research data to determine the nature and strength of the relationship between specific environmental pollutants and human health. The endpoints for these assessments are cancer and other toxicity. Heart and lung are important target organs for toxic effects. This function is one of the key mechanisms for translating research results into regulatory decision factors. The risk assessment process operates at the forefront of science, blending mathematics with health and environmental sciences, and thus has generated a variety of research activities. Current research investigations include:

- Review of worldwide literature and updating of criteria documents for ambient air pollutants such as SO_x, NO_x, ozone and particulates, which have the lung as the primary target organ
- Review and revision of Ambient Water Quality Criteria documents on 129 priority water pollutants, which include over 40 carcinogens
- Reevaluation of methods for quantitative risk assessment for nongenotoxic agents (carcinogens) to reflect recent advances in knowledge of mechanisms of action
- Evaluation of present statistical methods for detecting or predicting toxicity interactions among chemicals in a mixture
- Analysis of numerical sensitivity of proposed cancer risk models to errors of tumor diagnosis
- Comparison of human and animal cancer studies to improve the prediction of human cancer risks from animal cancer bioassays

- Development of risk estimates assessment guidelines for mutagens and agents that cause reproductive effects
- Development of advanced methods for using human data in risk assessment, including effects on target systems from multimedia exposures
- Estimation of extent of exposure of people near toxic landfills, including estimates of release rates and transport
- Development of guidelines for performing exposure assessments.

Recent advances and research findings include:

- Improved understanding of numerical errors and uncertainties in low-dose cancer extrapolation models
- Compilation of experimental observations that offer support and justification for uncertainty factors used to reflect safety in risk assessment procedures
- Partial explanation of the effect of time-to-tumor information on cancer risk estimates
- Comparison of mammalian tests for mutagenicity
- Qualitative approach for hazard assessment based on several dose-duration combinations
- Alteration in serum chemistry in humans due to drinking water contamination by chloroform and the trihalomethanes
- Estimates of 2,3,7,8-tetrachlorodibenzo-p-dioxin release from landfills, its movement in surface water, and the resulting potential risk from eating contaminated fish.

Office of Pesticides and Toxic Substances

The concerns of this office are addressed by the Office of Pesticides Programs (OPP) and the Office of Toxic Substances (OTS).

In implementing the provisions of the amended Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), OPP ensures that registered pesticides do not cause unreasonable adverse effects to people or the environment. This determination involves balancing the risks and benefits of pesticide use.

OPP research programs that explore the relationships between pesticides and disease (including cancer more often than lung or heart disease), and that are intended to reduce the incidence of such disease, include:

- Exposure studies focusing on people and other environmental components
- Epidemiologic studies involving survey work in cancer in certain areas of the United States
- Monitoring for pesticide residues in various environmental media
- Biological effects studies, supplementing those provided by pesticide registrants, to determine the short- and long-term effects of pesticides on living systems
- Study of dietary food factors to determine average intake of pesticide residues.

OTS is responsible for the implementation of the Toxic Substances Control Act (TSCA). Based on this responsibility, the OTS engages in a number of programs to assess the potential hazards associated with the manufacture and use of chemicals. Section 10 of TSCA directs the Administrator to carry out programs of research development, collection, dissemination, and utilization of scientific data to aid in the evaluation of potentially toxic environmental chemicals. In addition to chemical effects on the environment, the OTS seeks to understand the relationship between environmental pollutants and human health effects, including cancer and other diseases.

Current programs related to the assessment of cancer hazard include:

- Assessment of a number of limited bioassays for predicting candidate chemicals to be tested in long-term bioassays of cancer in animals
- Investigation of the application of biochemical and immunological markers of carcinogenicity to animal testing
- Development of short-term tests predictive of cancer hazard associated with fibrous materials.

Programs related to human disease in general, including cancer, heart, and lung disease include:

- Development of testing methods to guide the assessment of hazard for specific health endpoints, e.g., cardiovascular or pulmonary pathology
- Acquisition and utilization of available data to assess the relationship between similar chemical structures and their observed or potential effect on health

- Investigation of chemical residues found in human tissue and evaluation of chemical exposures leading to their accumulation.

Basic research work in ORD, NIH, and the scientific community, in general, continues to produce data that are relevant to this question of environmental factors and human disease. From the OTS perspective, some examples are increased knowledge of biological and minerological characteristics associated with mineral and manmade fibers, isomer-specific effects of halogenated aromatics, specific toxicities associated with heavy metals, and mechanisms of environmental detoxification processes, to name a few.

The diseases of primary interest for research into the possible linkage between environmental factors and human disease are explicitly identified in TSCA and in the FIFRA regulations as carcinogenicity, mutagenicity, and teratogenicity. With this as a backdrop, our priorities are:

- Understanding mechanisms of these diseases with an emphasis on pharmacokinetic considerations
- Monitoring studies to determine the presence, magnitude, and similar trends in exposure to environmental pollutants
- Epidemiological studies to investigate the relationship between exposure to environmental pollutants and the incidence of human disease
- Development of reliable, low-cost tests that accurately predict the potential to cause disease in humans.

Office of Air, Noise, and Radiation

The Clean Air Act (CAA) is the legislative authority for the air regulatory program. This program is designed to protect human health by controlling the amounts of harmful air pollutants or precursors to such pollutants emitted in the atmosphere. In general, there are separate programs to control criteria and noncriteria pollutants. Criteria pollutants are those that tend to be more ubiquitous in the atmosphere and are controlled through progams designed to meet National Ambient Air Quality Standards (NAAQS), performance standards for new sources, and emission standards for new mobile sources. Noncriteria pollutants in the atmosphere tend to be more localized in nature and generally are traceable to specific emission sources. Noncriteria polutants are controlled through emission standards for specific source types.

To regulate any air pollutants, EPA must have a scientifically credible and defensible understanding of any adverse health effect associated with exposure to the pollutant. In the Office of Air Quality Planning and Standards (OAQPS), this understanding is ascertained primarily through:

- Community epidemiology studies
- Controlled human exposure studies
- Animal toxicology studies.

Seven criteria pollutants (carbon monoxide, nitrogen dioxide, ozone, sulfur oxides, particulate matter, lead, and hydrocarbons) have been identified to date and NAAQS established. A major focus of the criteria pollutant health program is heart and lung disease. EPA is required under

Section 109 of the CAA to review the health basis of the NAAQS at 5-year intervals.

Eight noncriteria pollutants are designated in the CAA: one under Section 111(d)--sulfuric acid mist; and seven under Section 112--asbestos, beryllium, mercury, vinyl chloride, benzene, inorganic arsenic, and radionuclides. Regulations have been promulgated for four (asbestos, beryllium, mercury, and vinyl chloride) and are being studied for the remainder. A major focus of the noncriteria pollutant program is cancer. The importance of both criteria and noncriteria programs necessitates that the best science be available to support them.

Recent OAQPS studies and research findings include the following:

- Studies of potential noncriteria air pollutants have narrowed concerns from the several thousand substances in commerce and/or in the environment to less than 50 of greatest importance. Most of that group are of concern owing to a potential for carcinogenesis. This identification allows for much greater specificity of noncriteria air pollutants.

- A draft report entitled "Human Exposure to Atmospheric Concentrations of Selected Chemicals," was released for public review and comment in March 1981 (46 FR 15938 and 46 FR 28217). This study provided preliminary estimates of the number of people in the United States exposed to 33 high priority potential noncriteria air pollutants and the concentrations to which they are exposed. This information, along with effects levels, allows preliminary estimation of population risks.

- Study is underway to review and evaluate current information related to the possible association between air pollution and cancer.

- Study is underway to develop a risk assessment methodology for criteria air pollutants. This study is intended to provide better information concerning the probability of adverse effects and the severity of such effects.

- A study of available animal toxicology data (criteria air pollutants) is underway to determine the potential for extrapolating results to humans. This study is intended to allow more confident use of marginal epidemiological or clinical studies.

Research priorities in the area of criteria pollutants include the following:

- Epidemiology--Epidemiology studies should continue to provide important information to the criteria pollutant programs in the future. There is need to stimulate more research in this area both in the private sector and in other Agencies. Specific research needs are:

  --Study the effects of particulate matter and SO_2 in various atmospheres/situations
  --Study effects of O_3 on sensitive subjects (e.g., children)
  --Study the effect of repeated exposures to short-term peaks of NO_2.

- Clinical (Controlled Human) Exposure Studies--Studies of human biochemistry, immunology, and pulmonary mechanics should be conducted.

- Animal Studies--Studies are needed in several areas to expand our knowledge of the mechanisms and effects of criteria pollutants.

Research priorities in the area of noncriteria pollutants include the following:

- Epidemiology--As discussed above, research should be stimulated. Specific research needs include:

  --Comprehensive epidemiology studies for the principal suspect noncriteria pollutants (substances under active study by EPA include cadmium, acrylonitrile, several chlorinated organic solvents, nickel, and formaldehyde)

--Increased study of human exposures, activity patterns, and activity levels to help properly interpret epidemiology results

--Susceptible populations should be identified to ensure proper emphasis.

- Animal Studies--Increased research is needed to study the mechanisms of noncriteria pollutant toxicity, with emphasis on carcinogenesis. Carcinogens are potentially the most serious noncriteria pollutant problem. Because effects thresholds for carcinogens have not yet been identified, any exposure may pose some risk to humans. The limited number of past epidemiology studies as well as their generally poor sensitivity has necessitated reliance on animal test results. As such, knowledge of mechanisms for extrapolation from animals to humans and from high test concentrations to low ambient exposure concentrations is critical.

HEALTH AND HUMAN SERVICES

NATIONAL CANCER INSTITUTE

The National Cancer Institute is responsible for a number of programs aimed at identifying environmental carcinogens, assessing the relationships between these carcinogens and cancer incidence, and prevention of cancer through research and educational programs.

The Division of Cancer Cause and Prevention is responsible for planning and conducting the Institute's program of coordinated research on cancer causation and prevention. The Division supports both intramural laboratories and branches and extramural programs that seek to elucidate the mechanisms of cancer induction at each step of the cellular process from initiation to transformation of normal cells to malignant cells. The overall purpose of these studies is to provide information for reversing, interrupting, or preventing this process before the development of clinical disease.

To accomplish these goals, investigators pursue fundamental studies on normal and malignant cells and on carcinogens or procarcinogens, such as viruses and chemicals, using the disciplines of cellular and molecular biology, immunology, biochemistry, and microbiology, and epidemiologic studies of human populations to identify risk factors predisposing to various cancers, using the disciplines of clinical medicine, genetics, mathematics, and biometrics.

Excellent model systems are available to scientists studying the effects of exposure to a diversity of potentially carcinogenic factors in the environment. Much fundamental information has been obtained studying tumor viruses that induce cells to become malignant. These viruses provide tools for understanding how cellular genes and their products convert a normal cell into a tumor cell. Investigations in the area of biological carcinogenesis have shown that viral information present as nucleic acid sequences in the genes of normal cells and replicating with them may be intimately involved in the development of cancer. Triggered by chemical carcinogens, radiation, hormones, aging factors, and other influences, these highly conserved viral sequences may direct the synthesis of proteins responsible for malignant transformation of the cell. The work is conducted on animal and human cancers under several general categories, including virus-cell interactions, virus-host interactions, and molecular pathways of viral replication.

Similarly, chemical carcinogens, both synthetic and naturally occurring, provide a diverse group of chemicals with cellular and tissue selectivities that influence transformation and progression from the normal to the malignant state. Studies in the area of chemical/physical carcinogenesis cover a broad range of approaches with emphasis on the mechanisms of action of chemical and physical agents. Investigators have focused on the effects of carcinogens on cell structure and function, the relationships between molecular structure and carcinogenic activity, enzyme systems associated with the metabolic activation of procarcinogens to carcinogenic forms, the effects of the binding of carcinogens to DNA, and systems that repair DNA damage. Other relevant efforts include investigation of the role of various factors in the environment of the cell; for example, promoters, hormones and growth factors, which may be required for the progression of the "initiated" cell to the malignant state.

Finally, studies on the natural history of cancer in humans and on the incidence of cancers in different geographic locations help to identify causal associations of various intrinsic and extrinsic risk factors with various cancers. In view of the increasing importance of nutrition and lifestyle in the causation or prevention of cancer, in particular the role of vitamins and trace elements in the diet, alcohol consumption, and smoking, special emphasis has been given to projects that may have more immediate health implications. Many studies deal with determining mutagens/carcinogens in foods, natural inhibitors in foods, or assessing the carcinogenic components of cigarettes, and the influences of the total smoking experience. In addition, major studies on cancer incidence, mortality and survival in the United States, cancer incidence in the workplace, effects of low-level radiation, and environmental pollutants in air, water, and soil are under investigation.

Activities of the NCI of interest to the Task Force include a number of collaborative efforts with many Federal Agencies and private organizations concerned with the identification and control of carcinogenic agents in the general environment and workplace. One example of such activities includes the NCI/EPA Collaborative Program on Environmental Carcinogenesis and the NCI/NIOSH Collaborative Program on Occupational Carcinogenesis. Approximately 100 projects have been supported under these agreements thus far and include many areas of experimental, epidemiological and occupational carcinogenesis. The coordination, monitoring, and guidance of these programs are provided jointly by staff of the respective Agencies.

Frederick Cancer Research Facility

Activities supported by the NCI at this facility relevant to environmental aspects are conducted mainly in the Chemical Carcinogenesis Program. Research interests include basic research in chemistry, biochemistry, metabolism, and carcinogenesis studies of N-nitrosamine derivatives and polycyclic aromatic hydrocarbons, as well as investigations on specific cellular aspects of chemical carcinogenesis.

Division of Resources, Centers, and Community Activities

The Cancer Control Program has several programs aimed at reducing environmentally caused cancer. These include an occupational cancer effort directed toward worker education. The dissemination of preventive cancer information is being accomplished through a cancer communication network program located at a number of Comprehensive Cancer Centers throughout the United States. There are Smoking and Health projects involving such activities as self help approaches to smoking cessation and reducing smoking in populations at high risk, including adolescent and worker populations.

The Cancer Control Research Units (CCRU) and the Cancer Control Science Program are two new major research efforts about to be initiated. Their goal is to study effectiveness of cancer control interventions in defined populations relating to personal and lifestyle factors such as diet, smoking, and other environmental factors. Behavioral studies are being conducted which are aimed at reducing worker exposure to environmental carcinogens. The Radiologic Physics Centers are conducting a program to improve image quality and to reduce radiation dosage in diagnosis and treatment of cancer. In addition, they are actively supporting a program to ensure safety and quality control in medical X-ray equipment.

Recent Advances and Research Findings

Over the past 5 years there have certainly been a number of advances in our understanding of the relationship between environmental factors and the risk of various malignancies. These advances include:

- Animal studies have confirmed that agents strongly suspected of being carcinogenic in human populations are usually carcinogenic in animal tests.
- Cultures of cells obtained from humans with enhanced susceptibility to cancer also show enhanced susceptibility to mutagenesis by various carcinogenic chemicals.
- Human cells and tissues in culture show qualitative patterns of metabolism of carcinogenic chemicals similar to those of animal cells and tissues known to be sensitive to carcinogenic effects of these agents.

- Animal models for major forms of human cancer have been developed, specifically models for colon, breast, ovarian, pancreatic, prostatic, and bladder cancer.

- The importance of diet as a major environmental factor that can modulate human carcinogenesis has been shown.

- A link has been shown between smoking and cancer of the lung; smoking and cancer of other sites, such as the bladder; smoking and the development of emphysema; smoking and the risk of increasing oral cavity cancer; and smoking and the development of pancreatic cancer.

In addition, the disciplines of epidemiology and biometry have contributed to a number of these findings.

In the area of descriptive epidemiology, a number of observations have suggested productive avenues of research into the environmental causes of cancer and have allowed a monitoring of changes in the rate of malignancy as they may relate to changes in our environment. Specifically, the Surveillance Epidemiology, and End Results (SEER) Program of cancer incidence registries that covers approximately 10 percent of the U.S. population has identified a variety of trends in human cancer in our society. Rising rates for cancers of the lung, urinary bladder, pancreas, body of the uterus, and non-Hodgkin's lymphoma, multiple myeloma, and malignant melanoma have all led to testable hypotheses about changes in the environment that may be responsible for these increases. The lack of any substantial increase for a number of other sites, including cancers of the colon and breast, have led to hypotheses concerning the lack of any impact on these tumors of a variety of changes in environmental exposures. Declines in the rates of several tumors, including stomach cancer and cancer of the uterine cervix, have also led to testable theories about changes in environmental exposures over time that may have been responsible for these decreases.

The nonrandom geographic distribution of mortality from a variety of cancers has also been used to develop clues to environmental causes. Specifically, the excesses of lung cancer on the Gulf and Southeast Atlantic Coast and the excesses of bladder cancer in areas of the Northeast and urban Midwest have suggested a number of different industrial causes for these unusual disease distributions. Similarly, north-south differences in colon cancer mortality, Northern urban excesses of esophageal cancer, and a rural Southeastern excess of mouth cancer have all led to specific testable hypotheses concerning nutritional and tobacco-related etiologies for these malignancies.

The area of analytic epidemiology, which investigates potential causes of cancer by aggregating information on specific individuals with and without the disease, has followed up on the various descriptive findings outlined above, as well as provocative findings from clinical observations and laboratory studies, to identify a number of environmental causes of cancer. In the area of occupational studies, work in the shipyards during and after World War II has been identified as one of the major reasons for the coastal excesses of lung cancer noted above. The Northeastern and urban Midwestern excesses of bladder cancer have been related to a variety of occupational exposures in chemical and other manufacturing industries. Excesses of brain malignancies may be related to work in petroleum refineries, and the risk of leukemia has been linked directly to exposure to benzene in the petrochemical industry.

In epidemiologic investigations of radiation, a number of studies of various groups exposed to intermediate or large doses of ionizing radiation have been performed in order to achieve better estimates of the dose-response relationships between radiation and cancer at a variety of sites so that better approximations of low-dose effects can be made. In particular, the combination of results from atomic bomb survivors, patients treated for tuberculosis who received multiple fluoroscopic examinations, and women treated with radiation for postpartum mastitis has allowed a fairly precise definition of the dose-response curve for radiation exposure and the risk of breast cancer.

In evaluation of long-term effects of therapeutic drugs, a number of observations have been made over the past 5 years. The use of estrogens for menopausal symptoms has been firmly linked to cancers of the body of the uterus and long-term use of these same preparations is becoming more firmly related to an excess of risk of breast cancer. Use of sequential oral contraceptives has been related to an increased risk of cancers of the body of the uterus. Overall, use of the combination oral contraceptives has not been related to an excess of malignancy, and some evidence has been developed implicating these drugs as being associated with a reduced risk of cancers of the ovary and endometrium.

Analytic evaluations of dietary and other nutritional aspects of cancer have suggested a protective effect against various malignancies for carotene, vitamin A, and perhaps a number of other micronutrients. A variety of studies have also increased concern about the role of dietary fat in the etiology of a number of tumors, particularly those of the colon and breast.

In addition, alcohol abuse has been consistently linked with tumors of the upper GI tract. Conversely, recent studies have indicated that the use of another dietary agent, artificial sweeteners, while perhaps carcinogenic in animals, is not associated with a large increase in cancer risk to humans.

Investigations into potential infectious causes of cancer have recently developed substantial evidence that at least a portion of some tumor sites may be related to exposure to specific infectious agents. Included among these is the relationship between hepatitis B infection and subsequent primary cancers of the liver, herpes virus type 2 as a risk factor for cervical cancer, the identification of a new virus in relation to a specific form of T-cell leukemia and lymphoma, the ongoing concern over the role of Epstein-Barr (EB) virus in Burkitt's lymphoma, as well as tumors of the nasopharynx, and the possibility of an infectious origin for the recent outbreak of Kaposi's sarcoma among young male homosexuals. Finally, a number of studies of familial aggregation of malignancy and the occurrence of malignancy in association with a variety of genetic diseases has clarified the role of various host factors in the expression of cancer due to some environmental exposures.

In summary, both laboratory studies and epidemiologic investigations utilizing established resources as well as ad hoc studies have produced a substantial number of recent advances that have elucidated the relationship between various environmental factors and the risk of malignancy.

Research Priorities

NCI's relative priorities for research into the possible linkage between environmental factors and human disease include:

- Elucidate the mechanism of chemical carcinogenesis.
- Define the role of tumor promoters or other non-carcinogenic agents that enhance the expression of transformed cells.
- Develop early preneoplastic markers for each target organ to aid in diagnosis of preneoplasia.
- Develop sensitive assays to monitor biological effects of exposures to specific agents. The use of antibodies to carcinogen-DNA adducts is particularly promising for this purpose.
- Identify individuals with different ability to activate environmental carcinogens. Identify factors that can modify the processes involved in the induction and progression of chemically induced cancer. Identify individuals who have had an exposure to potentially harmful environmental compounds and the subsequent biological interaction.

Also in the area of the epidemiologic investigations of cancer etiology, the NCI will be pursuing a number of research priorities relating to the environmental causes of cancer. Included are the following:

- Continued monitoring of incidence and mortality patterns for cancer by age, time period. race, sex, and geographic locale in order to identify emergent problems and changes in risk that might have environmental determinants.
- Pursuit via follow-up and case-control studies of the risks involved in relatively large exposures to identifiable environmental agents that are known or suspected carcinogens. Included are evaluations of occupational exposures, ionizing and nonionizing radiation, medicinal agents, and other environmental exposures resulting from activities associated with various lifestyles.

- Exploratory studies of high- and low-risk groups to attempt to identify exposures that may be responsible for the unusual cancer risk experienced by a particular group.

- Special emphasis will be placed on direct assessments of the risk of malignancy associated with general environmental exposures (i.e., air and water pollution), and specific components of the diet. These assessments of the influence of general environmental and nutritional determinants will require a particular focus on development of new and more precise ways of measuring the exposures of concern.

- Another priority item for research will be to incorporate a variety of biochemical and metabolic measurements into the epidemiologic assessments of relationships between various exposures and disease. This approach of biochemical epidemiology will be used to more precisely measure exposures, to detect intermediate outcomes, and to identify the specific mechanisms whereby a particular exposure may cause a certain disease.

NATIONAL HEART, LUNG, AND BLOOD INSTITUTE

During the last 10 years, the Epidemiology and Biometry Program of the Division of Heart and Vascular Diseases, NHLBI, has pursued several studies in relation to environmental pollution and heart disease. These have included: the Seattle Study of Trace Element Exposure, the drinking water component of the Health and Nutrition Examination Survey, and the Boston Study on Relation of Water Constitutents to Health; a study of artificial fluoridation in relation to mortality from cardiovascular and other diseases; and investigations of methodological techniques for analyzing trace metals in water and biological samples. In addition, the NHLBI has participated in task forces, working groups, expert committees, and international meetings on the subject of environmental factors and health. The sessions have produced a number of recommendations for the Institute and the scientific community. The most recent--and one of the most comprehensive statements--on the major environmental factors related to heart disease is contained in the report from the American Heart Association (AHA) Task Force on Cardiovascular Disease, which appeared in Circulation 1980. Parts of the summary of the AHA report are reprinted in Chapter 3 of this report. The AHA report covered the areas of water hardness, trace elements, inhalant occupational exposures, carbon monoxide, noise and radiofrequency, and physical and psychosocial stresses.

Several working groups have also been convened by the NHLBI that have addressed this issue and that have made a variety of recommendations. These are contained in the report of the Working Group on Heart Disease Epidemiology and in the NHLBI 10-year Update, which will be completed sometime later this year. The Institute is currently engaged in several related activities. These include the continuation of studies of water hardness and cardiovascular mortality using small-area data and city data that had been assembled previously, studies of occupational risk factors using a link between the current population survey files and the National Death Index, which is undergoing a feasibility study at the present time; and correlation of county mortality data with available environmental indices. The degree to which these studies can be expanded in the future will depend very much on the priorities ascribed to other research areas in the Institute and the availability of total Institute funding.

Research related to pulmonary diseases includes studies of: the effects of toxic environmental chemicals and tobacco products on the lung; comparison of the occurrence of obstructive lung diseases in areas of high versus low pollution; environmental factors that produce airway diseases; the occurrence of subclinical respiratory disease; the pathogenesis and pathobiology of mineral pneumoconiosis; the effects of pollutants on organotypic lung cultures; the effects of ozone on lung function; the biological effect of ozone, nitrous oxide, nitrogen dioxide, and tobacco smoke; airborne metals and lung permeability; epidemiologic studies of chronic lung diseases; and comparison of genetic and environmental influences on lung disease.

Recent advances and research findings in the area of pulmonary disease include the identification of a new pulmonary syndrome in workers in plants where plastics are manufactured. Trimellitic anhydride, a conjugating agent used in the manufacture of plastics, when inhaled, produces a debilitating and potentially life-threatening "pulmonary disease-anemia syndrome." Studies are currently in progress to determine the immunologic characteristics of exposed workers who develop the syndrome and those who remain asymptomatic.

Another recent finding may make it possible to test pigeon breeders for hypersensitivity lung disease (pneumonitis) using a simple test of cellular immunity in lung lymphocytes. New findings in the study of asbestosis have also suggested that the individual's immune system may be a critical factor in the development of asbestosis.

Environmental pollutants now include smoke from cigarettes, which is now being recognized as deleterious to the nonsmoker who is subjected to it. This so-called "passive" smoking has been shown to have a detrimental effect. Children with smoking parents develop a higher incidence of respiratory symptoms and hospital admissions than children with nonsmoking parents.

Furthermore, it is now known that children who experience respiratory damage early in life are at increased risk of developing chronic obstructive pulmonary disease as adults.

NATIONAL INSTITUTE FOR OCCUPATIONAL SAFETY AND HEALTH

The primary responsibility of the National Institute for Occupational Safety and Health (NIOSH) is to provide research and standards-setting support to the Occupational Safety and Health Administration under the Occupational Safety and Health Act of 1970 and to the Mine Safety and Health Administration under the 1977 Amendments to the Federal Mine Safety and Health Act.

NIOSH's current programs are divided into four major areas: Criteria Documentation and Standards Development, Research, Technical Assistance, and Manpower Development.

Criteria Documentation and Standards Development

NIOSH provides recommended health and safety standards in the form of criteria documents to the Secretary of Labor for promulgation and enforcement. The order of hazards selected for criteria development is determined by a NIOSH priority system based on severity of response, population at risk, carcinogenicity, availability of an existing standard, and advice from Federal Agencies and involved industry, organized labor, and professional groups. For a selected hazard, available scientific, medical, and engineering research information is systematically gathered and collated. Throughout the preparation of a criteria document, extensive and broadly based review procedures are carried out with reviewers selected not only from labor and industry, but also from universities, research organizations, professional groups, and various Federal and state Agencies.

Research

The largest effort within NIOSH, both in terms of dollars and personnel, is directed at applied occupational health and safety research. Most of this research addresses the development or modification of criteria for recommended occupational safety and health standards. Other research is directed at assessing interactions between chemical and physical agents, at developing new monitoring techniques and analytical methods, and at methods of diagnosing and preventing specific occupational diseases. Examples of NIOSH's research effort related to the Task Force's mandate include:

1. Surveillance, control technology assessment, and laboratory research aimed at identification and prevention of occupational cancer
2. Development of sensitive and specific diagnostic tests for occupational disease
3. Identification of dose-response relationships to ensure safe working conditions in industries
4. Development of personal protective equipment to reduce exposure to industrial chemicals
5. Studies to evaluate selected workplace environments (coal mines, cotton processing, as examples) in order to assess the adequacy of existing exposure standards
6. Epidemiological and industrial hygiene studies related to conventional and new energy sources.

Technical Assistance

NIOSH provides a variety of technical assistance to employers, employees, universities, and professionals in the field of occupational safety and health. These include:

1. Medical examinations and autopsies of coal miners
2. Maintaining a program to certify "B" reader physicians who provide medical interpretations of chest radiographs submitted to the Institute under the provisions of the miner examination program mandated by law
3. Testing and certification of personal protective equipment and hazard measuring devices (gas detector tubes, noise level meters, etc.)
4. Health hazard evaluations.

Manpower Development

NIOSH currently offers a series of 39 technical training courses for representatives from Federal Agencies, state and local governments, private industry, and unions. NIOSH also provides training project grants to educational institutions for specific occupational safety and health training programs. In 1976, NIOSH initiated the Educational Resource Center concept. These Centers, funded through training grants, provide for occupational medicine and associated professional occupational health and safety training. The Institute also participates in the Epidemiologic Intelligence Service (EIS) Program by providing on-the-site training in various aspects of occupational medicine.

Recent Research Findings

NIOSH research findings in 1981 include:

- A behavioral teratology study of the interaction between maternal exposure to 2-ethoxyethanol (2-EE), an industrial solvent, and ethanol showed ethanol enhanced the teratogenic effects of 2-EE.
- A neurobehavioral study of viscose rayon workers, exposed to carbon disulfide showed that workers having documented historical CS_2 exposure at the current threshold limit value (20 ppm) or less, showed small, but statistically significant impairments in peripheral nerve function and some behavioral tasks.
- A study of workers exposed to a new plastic foaming agent (lucel-7) used to make fibrous glass reinforced bathtubs showed an increased risk of peripheral neuropathy.
- A study of workers previously found to have neuropathy due to exposure to ESN, a chemical catalyst, showed significant long-term disability (bladder and sexual dysfunction).
- A study of workers at a uranium milling facility showed an increased risk of renal tubular damage.

Research Priorities

NIOSH's relative priorities for research into the possible linkage between environmental factors and human disease include occupational cancer so as to prevent a major cause of workplace mortality, occupational respiratory disease and its control, and reproductive effects resulting from workplace exposure.

Cancer research priorities include:

- Assessment of carcinogenic potential of complex mixtures, modifications of carcinogenesis by promoters, and the etiology of the carcinogenic process in various workplace environments
- Epidemiologic investigations to determine whether or not specific occupational exposures or work within certain occupational groups in general are associated with an increased risk of developing cancer.

Respiratory disease research priorities include:

- Laboratory-based research on physiological mechanisms and the effect of various challenge agents on lung mechanics and pulmonary function
- Morbidity and mortality studies to assist in the development of dose-response information
- Mortality and case control studies of nonmalignant respiratory disease.

Reproductive effects research priorities include:

- Conducting reproductive toxicology studies
- Developing mutagenic monitoring systems for the workplace environment
- Conducting epidemiologic studies of reproductive failure and parental exposure
- Identifying groups of workers potentially exposed to teratogens in the workplace.
- Developing in vitro assay systems to study the mutagenic activity of workplace chemical complexes and mixtures
- Developing human mutagenic monitoring systems that include urine analysis and cytogenic and gene mutation assays.

NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES

The National Institute of Environmental Health Sciences (NIEHS) supports and conducts research aimed at the development of knowledge basic to understanding of the processes by which human health can be adversely affected by the environment. This research concentrates on recognizing, identifying, and investigating the environmental factors that may have deleterious effects on population groups, on quantifying those effects, and on understanding the mechanisms of action of toxic agents on biological systems. These efforts provide information that serves those charged with preventing and treating environmentally related disease, as well as Agencies responsible for regulating exposure to hazardous substances. All these activities are relevant to prevention of environmentally related cancer, heart, and lung disease, covering a spectrum from chemical identification and analysis of specific environmental agents to epidemiological studies of human populations. They include an emphasis upon development of environmental health science resources through extramural center grants and research training programs.

The most significant change since the First Annual Report of the Task Force, August 7, 1978, was the approval by the Secretary, HHS, in July 1981, of a major reorganization and the transfer of the Carcinogenesis Testing Program from the NCI to the NIEHS. The reorganization established four distinct program areas within NIEHS: (1) the Extramural Program; ((2) the Intramural Research Program; (3) the Toxicology Research and Testing Program; and (4) the Biometry and Risk Assessment Program.

Extramural Program (EP)

The Extramural Program emphasizes the development of environmental health science resources through extramural grants and research training programs. These research support efforts can be divided into two primary program areas:

Characterization of Environmental Health Hazards

Research in this area seeks to identify and measure hazardous biological, chemical, and physical environmental factors and the transformed products that result from their interaction in biological systems. This includes:

- Development of sensitive and accurate techniques that allow the analysis and characterization of potentially toxic substances
- Work on determining how and at what rates environmental agents enter the body, are stored, metabolized and excreted
- Development of new test methods for detecting the effects of agents on biological systems
- Development of methods for assessing and predicting consequences of exposure to environmental agents in the human population.

Biological Response to Environmental Health Hazards

Research in these areas seeks to understand the biological and biochemical response to environmental forces. Once the disease process is understood, steps can be taken to avoid, alter, or possibly correct these adverse biological effects that lead to morbidity and mortality.

This research also provides information regarding the relative susceptibility of individuals who are at higher risk and contributes to a developing capability to predict long-term chronic effects of environmental contaminants.

The EP also is responsible for the environmental health research and manpower development resources program. NIEHS support in this program area provides long-term stable core support for broadly based multidisciplinary research and training programs focused on a variety of environmental health problems. This support is provided through university-based Environmental Health Science Centers and Marine and Freshwater Biomedical Centers. These multidisciplinary Centers serve as national resources for research in such health problems as air, water, and food pollution; occupational and industrial health and safety; heavy metal toxicity; agricultural chemical hazards; the relationships of the environment to cancer, birth defects, behavioral anomalies, respiratory and cardiovascular diseases, and diseases of other specific organs; and basic aspects of toxicity mechanisms, body defense mechanisms, and the influence of age, nutrition, and other factors in chemically induced injury and disease. The manpower development program supports research training at the pre- and postdoctoral levels in environmental toxicology, epidemiology, pathology, and mutagenesis.

With respect to the Task Force's specific interests, extramural research supported by NIEHS extends from studies of biological effects of known and suspected carcinogens and mutagenicity/carcinogenicity correlations to epidemiological surveys to assess insult from environmental exposures. The EP supports grantees studying environmental aspects of cardiovascular diseases, ranging from impacts of pollutant exposures on erythrocyte function to the possible role of environmental mutagenesis in the pathogenesis of arteriosclerosis. Population supported studies are exploring the association between incidence and severity of cardiovascular sequelae to acute and chronic exposures to high and low levels of environmental agents alone and in multiple combinations. There is a major epidemiological study being supported that is looking at air pollution in six cities and attempting to determine whether there is a correlation between particular types and levels of air pollution and respiratory problems.

Intramural Research Program (IRP)

The Intramural Research Program develops knowledge of how environmental chemicals damage biological systems. It aims to provide the kinds of information that will have explanatory and predictive value in utilizing experimentally determined toxicity. The conduct of this research requires the development of sensitive chemical analyses that employ advanced spectrometric and physical separation techniques. Application of these methods permits characterization of the hazardous chemicals to which populations are exposed, definition of the chemical transformations as they lead to toxic effects, and identification of specific molecular changes in cells and tissues that are the consequence of damage by toxic chemicals.

The expression of toxic chemical damage in organ systems is frequently detected long after exposure, at high doses of chemicals, and after an irreversible effect has been achieved. By developing knowledge of molecular and cellular events that occur closer to the biological onset of disease and by identifying sensitive criteria of damage that can be used to detect harmful exposure, the utility of experimental toxicological systems will be increased. In addition, a more complete understanding of the detailed abnormal processes that correspond or differ in animal and human cells will increase the confidence of an experimentally based analysis of risk. In this context, the IRP focuses its efforts on the study of genetic mutations, neurobehavioral effects, reproductive abnormalities, and cellular toxicology of the lung.

Of particular relevance to the charge of the Task Force is the IRP Laboratory of Pulmonary Function, where the lung as an avenue of exposure and as a principal site of damage from environmental chemicals is experimentally approached through several projects in cellular toxicology. Epithelial cells that line airways have been maintained for long periods in cell cultures supplemented with hormones. These cells retain the capacity to develop cilia and to secrete mucous protein. Such cell cultures offer direct approaches to studying carcinogenic and toxicological processes. Substances that promote but cannot initiate cancers can produce abnormal cells and loss of growth control. Early stages in the neoplastic progression of these cells are being characterized and correlated with abnormal chromosome number and morphology. Studies of several cell types have shown that the rates of neoplastic transformation and mutation are not necessarily related and that transformation is more regularly associated with an abnormality of chromosome number.

The transformation of foreign chemicals to active compounds that are the proximate causes of biological damage has been characterized in purified cell types that have been isolated from rabbit lung; two different cell types have shown clearly different metabolic pathways for polycyclic aromatic hydrocarbons. Purification and immunological detection of the cytochrome oxidation pathways have delineated several distinct forms of the enzymes that bring about these changes and these pathways vary with cell type. These studies are being correlated with observations on the amount of the activated polycyclic hydrocarbon that is linked to DNA in the cell. Studies such as this aim to explain the induction of cancer in various cell types and the differences in incidence and outcome of effects in different species.

Toxicology Research and Testing Program (TRTP)

The Toxicology Research and Testing Program is essentially the NIEHS contribution to the National Toxicology Program (NTP) and constitutes the NIH component of the NTP, composing approximately 87 percent of the total NTP resources. TRTP emphasizes three major areas: test methods development/validation, toxicological characterization of chemicals, and testing of chemicals for potential adverse effects including carcinogenic, genetic, and reproductive outcomes.

Newer or refined test methods are being explored in order to develop more accurate, specific, and rapid procedures to characterize and predict potential toxic effects for humans from chemical exposures.

It should be noted that, with regard to the Task Force's interest, the Program continues to emphasize and refine the "standard" carcinogenesis bioassay. Since the early 1970's when the National Cancer Institute's

Carcinogenesis Bioassay Program (now part of the NIEHS) initiated the long-term testing of chemicals for carcinogenic potential in laboratory animals, 241 chemicals have been investigated: 116 chemicals (48 percent) have been evaluated as being positive, 102 (42 percent) as being negative, and 23 (10 percent) as being equivocal.

The TRTP emphasis on testing, test development, and associated research does not imply flaws in traditional toxicology and regulatory requirements, but reflects rapid advancements in testing methodology and expanding boundaries of scientific knowledge.

Biometry and Risk Assessment Program (BRAP)

The Biometry and Risk Assessment Program, which is the newest of the major program areas at NIEHS, is an outgrowth of the old Biometry Branch that was previously located within the Institute's Intramural Research Program. BRAP plans and conducts basic and applied research in the area of health risk assessment, biostatistics, biomathematics, and epidemiology. The elevation of these activities to program status reflects the Institute's growing interest in the various research issues and practical problems associated with the assessment of potential human health risks incurred as a result of exposure to hazardous environmental agents.

BRAP staff collaborate with the scientists involved in the Toxicology Research and Testing Program, assuming responsibility for data management and statistical analysis. BRAP also provides statistical, mathematical data processing, and computer engineering support to the other programs of the Institute, as well as assisting the Office of the Director in addressing specific health issues that bear on the welfare of the general public.

In the specific area of cancer epidemiology, attention has been directed toward:

- Assessing the impact of occupational asbestos exposure during and after World War II on present and future overall cancer risk
- Evaluating secular trends in the distribution of breast cancer risk factors in Hiroshima and Nagasaki (Japan)
- Completing a case-control study of the relationship of trace elements such as selenium to the onset of skin cancer
- Analyzing renal cancer mortality patterns in (U.S.) counties where a significant proportion of the population is employed in lead-related industries
- Initiating a case-control study of adult cancer risk and maternal smoking history during pregnancy.

Recent Research Advances

Genetic Toxicology

In an effort to define how hazardous chemicals interact with coding and noncoding regions of DNA, NIEHS research emphasizes cloning and molecular characterization of genes, which will provide the basis for predicting the consequences of somatic and germinal mutations. Cloning of specific genes in Drosophila and the molecular characterization of transposable DNA elements have demonstrated how these elements become inserted and increase mutation rates manyfold at gene loci.

The Institute has a genetic toxicology testing effort using a combination of test methods that evaluates approximately 300 chemicals per year. Promising in vivo and in vitro methods are being validated through selection of chemicals that represent major chemical classes.

Grant-supported researchers using the Ames/Salmonella microsome test system are examining 46 dyes, pigments, and colorants for mutagenicity. These substances are used extensively in industry and have not previously been subjected to this kind of testing.

Reproductive Toxicology

An animal model has been developed for assessing risks from the human transplacental carcinogen diethylstilbestrol (DES). The model predicted the genital abnormality, retained testes, subsequently found in human males, and abnormalities of the Fallopian tubes seen in DES-exposed women. The relationship of adenosis and vaginal carcinoma was also shown previously in this work. This work has provided the basis for the study of a variety of chemicals with estrogenic properties.

The Institute developed and implemented an integrated fertility and reproductive assessment program that is oriented toward detecting effects mediated through both male and female exposure. Initiatives that assess utility of short-term screening procedures are in progress.

Grant-supported studies in the mouse, as well as of exposed human populations, indicate that elimination of mercury after exposure to methylmercury may be affected by stage of development and diet. The ability of methylmercury to cross the placenta and to be secreted in breast milk are important considerations for hazard evaluation to fetus and suckling infant.

Toxicological Characterization

The technique of fast atom bombardment has extended the range of analytical mass spectrometry to intermediate molecular weight compounds, making it an even more discriminating and sensitive method for detecting, measuring, and separating toxic substances.

Research studies with polybrominated biphenyls (PBBs) confirmed the carcinogenic potential in rats and identified similar effects in mice. The studies further indicated that the toxic liver lesions are progressive even after exposure to the chemical is terminated.

Dichlorobenzidine (DCB), used commercially in the United States primarily in the manufacture of pigment, is known to be a potent carcinogen in animals and is assumed to be carcinogenic in man. Studies using animals with ligated bile ducts found no radiolabelled DCB in the feces, indicating that no process other than biliary excretion results in the elimination of the material into the gastrointestinal tract, where hydrolysis and absorption of the substance take place, events required for the process of carcinogenesis to begin.

A testing program that assessed carcinogenic potential of a chemical in 2-year tests with rodents has been transformed into a program that also characterizes other major toxic properties of a chemical, i.e., effects on liver, lung, kidney, and fertility. Further, the testing program develops data that permit better assessment of toxic effects that may be related to magnitude and duration of exposure or are peculiar to a given sex or test species or are generally applicable to a group of chemicals within a chemical class. These types of data enhance our ability to assess more effectively potential human risk.

Pulmonary Studies

Tracheal epithelial cells from the rat have been established in culture and the stages of neoplastic transformation caused by chemical carcinogens studied for changes in cell morphology and growth rate. These systems are being studied to identify the molecular and genetic changes that accompany neoplastic transformation in pulmonary epithelial cells.

A major prospective epidemiological study of air pollution and respiratory disease is continuing in a six-city investigation. This study relates respiratory health effects to particulates and sulfur oxides. Both indoor and outdoor monitoring for SO_2 and NO_2 are features of the study.

An epidemiological study of chronic obstructive respiratory disease (CORD) and functional respiratory impairment correlated with long-term exposure to photochemical oxidants suggests that both current smokers and those who have never smoked residing in an area exposed to high levels of photochemical oxidants have poorer lung function than current smokers and people who have never smoked living in an area exposed to low levels of photochemical oxidants or to high levels of SO_2, particulates, and hydrocarbons.

Risk Estimation

An estimation of the quantitative impact of including pharmacokinetic considerations in the low-dose risk extrapolation process for carcinogenesis has been performed. Results suggest that introducing pharmacokinetic parameters into the modeling process can significantly improve the fit of the model to the experimental data in some cases.

Clinical data on growth, morbidity, and development are being gathered on 900 North Carolina children enrolled in a birth cohort study of the potential adverse effects associated with infant exposure to environmentally contaminated breast milk. Results to date indicate a very high prevalence (90 percent) of maternal breast milk contaminated with polychlorinated biphenyls and DDE, a metabolite of DDT. This study should lead to development of methodology for investigating effects of low levels of pollutants on humans.

Research Priorities

Research can increase our understanding of the basic mechanisms through which humans take up, modify, absorb, and excrete chemicals, and can, therefore, lead to the development of principles for determining what chemicals are hazardous to humans, and how they express their toxicity. Priority areas include:

Food Mutagens

Research being sponsored by NIEHS at the Lawrence Livermore National Laboratory and the University of California-Berkeley already has produced significant findings about the relationship between the time and temperature used to cook meat and types of mutagens produced during the process. Agents that are mutagenic to humans may be present in food from three sources: as natural components, as additives or contaminants, or as a result of the processing or cooking of the food. In 1978, Commoner found that mutagens were produced during the frying of hamburger and the boiling of beef stock. These mutagens have turned out to be different from those formed by charring meats or by charbroiling. Areas for study include the following:

- The nature and mechanism by which mutagens are produced in cooking
- The chemical structure of the principal mutagens
- Quantification of the mutagen formation using a standard bacterial assay, and assessment of the genetic toxicity of the mutagens in in vitro and in vivo short-term mammalian assays
- Estimation of the risk to humans from eating foods containing mutagens
- Consideration of possible strategies to prevent mutagen formation or control the risk from consuming these foods.

Genetic Damage in Mammalian Cells

A research priority may be to develop and validate systems to identify and monitor genetic effects in human populations at risk from exposure to hazardous chemicals.

Human Carcinogen Data Base

Current methods for assessing carcinogenic potential of chemicals basically provide only crude qualitative information. A research priority is to identify methods that permit some quantitative estimate of risk and a general understanding as to what major processes are associated with a carcinogenic response to a specific chemical. There are approximately three dozen chemicals for which there is strong evidence of human carcinogenicity. Animal studies with these chemicals also indicate carcinogenic effects. Characterizing the specific response of these human carcinogens using current toxicology test methodology could provide insight as to the utility of various methods for detecting carcinogenic risk. Its greater long-term value could be to serve as a reference data base against which to compare the utility of emerging test methods.

Identification of Cellular Injury

A priority may be to develop a technology to permit identification of specific types of cellular injury due to chemicals, hopefully at dose levels that do not cause morphologic alteration.

Human Risk Estimation

The program in human risk estimation may be expanded into the area of demography and time trend analyses of vital statistics. Techniques from this approach are used to evaluate the impact on human health of occupational and general environmental conditions. Analyses linking health data with environmental containment levels could provide important insight into these new research issues, and the methodologies associated with this type of investigation need refinement.

Another priority is to develop our tools for estimation. Of particular importance are the development of methodologies in the noncarcinogenesis areas such as reproductive outcomes. Both biological modeling and experimental data base analyses could be undertaken.

Reproductive Toxicology

Improving understanding of molecular mechanisms in reproductive toxicity may lead to characterization of hormone-receptor interactions at the level of gene regulation and protein transcription. Such studies could include environmental factors that alter the determinants of gonadal sex, fetal gametogenesis, and reproductive tract differentiation.

NATIONAL CENTER FOR HEALTH STATISTICS

The National Center for Health Statistics (NCHS) has been responsible for national surveys of health for over 25 years. Its 14 major data collection programs produce morbidity and mortality data on a wide range of diseases, including cancer and heart and lung disease. These data are analyzed and published, resulting in a series of more than 600 reports that are distributed worldwide. In addition, computer data tapes are available to researchers for further processing and analysis. These data systems frequently provide basic data for use by other Federal Agencies in their research on the potential relationship between environmental factors and cancer and heart and lung disease. Data collection programs of special relevance to the research include:

- National Health Interview Survey
- National Health and Nutrition Examination Surveys
- Basic national, state, and county mortality data on an annual basis
- National Hospital Discharge Survey
- National Ambulatory Medical Care Survey.

These broad national data systems, together with other NCHS data collection activities, furnish basic national health statistics on morbidity and mortality, enabling the selection of populations with potential environmentally related diseases for further study. Monitoring of the effectiveness of public health programs for reducing disease and lowering mortality is made possible by the continuing availability of detailed health statistics.

Brief Description of Current NCHS Research Activities

Current NCHS research activities directed at or related to environmental factors include specific sections of surveys containing questions on environmental factors. The surveys involved are:

1. National Health and Nutrition Examination Survey (NHANES)

   This comprehensive survey includes several component surveys such as NHANES I; NHANES I Augmentation; NHANES I Epidemiologic Followup Survey; NHANES II; and Hispanic NHANES. All of these share a common purpose--collection and utilization of data obtained by physical examinations, clinical and laboratory tests, and related measurements. Two types of data are obtained--prevalence for specific diseases or conditions and also health-related measurements, such as blood pressure, visual acuity, and serum cholesterol. Among the many items of data collected are several that pertain to environmentally related diseases. These are described below within the component surveys.

   a. The NHANES I Augmentation Survey (1974-75) included a Water Sample Collaborative Study with the NHLBI and EPA. Its purpose is to determine possible relationships of bulk constituents, hardness, and trace metals in household tap water with certain risk factors of cardiovascular disease. The data will be analyzed for possible associations of these drinking water constituents with cardiovascular disease, cancer, hypertension, and some other conditions, such as arthritis, urinary problems, and neurologic abnormalities.

The first report, a detailed presentation of elements consumed through drinking water, is now in preparation. The second report of this NCHS series will emphasize the possible relationship of chemical elements in drinking water to blood pressure, hypertension, and serum cholesterol levels. These studies are being developed with Dr. Richey Sharrett, Epidemiological Branch, Division of Heart and Vascular Diseases, NHLBI.

b. The Hispanic Health and Nutrition Examination Survey (Hispanic HANES) began in July 1982 and will be completed by late 1984. The survey will include Mexican-Americans in the five southwestern states, Puerto Ricans in the New York area, and Cuban-Americans in the Miami area. As in the previous NHANES II, there will be samples taken of blood and urine to measure body burdens of lead, carbon monoxide, and selected pesticide residues and metabolites. These body burden levels will be published by selected demographic characteristics and correlations with these levels will be explored in relationship to variables such as smoking, drinking, and other health-related factors.

c. The NHANES I Epidemiologic Followup Survey (1982-83) will interview adults (ages 25-74) who were examined in the first National Health and Nutrition Examination Survey 1971-75. Funds are being provided by the National Institute on Aging, other NIH Institutes, and other Federal Agencies. The followup will focus on how factors previously measured in the earlier study relate to health conditions that have developed since that time. Specific items on the questionnaire that relate to environmental factors include questions on skin cancer, cigarette smoking, source of drinking water, occupational exposure to dusts, fumes, or vapors. All deaths of this population will be identified.

A search of vital statistics records will be made for all subjects who are "lost to followup." Deaths of the population will be monitored subsequent to interview using the National Death Index. Outcomes with long latency periods will be identified in this manner.

d. National Health and Nutrition Examination Survey II (NHANES II, 1976-80) continued the data collection efforts of NHANES I with some notable additions. Specific environmentally related data collected in this survey included levels of lead in whole blood; carbon monoxide levels in the blood (carboxyhemoglobin); pesticide residues in the serum (such as DDT, dieldrin, mirex, hexachlorobenzene, among others); and pesticide residues in the urine (such as pentachlorophenol, silvex, DMTP, among others); and a smoking and drinking history. It is planned to analyze these data to seek possible relationships between them and health and nutritional status, including environmentally related diseases.

2. National Natality Survey (NNS) and National Fetal Mortality Survey (NFMS)

The 1980 NNS was designed as a vital statistics followback survey. The 1980 NFMS is a parallel survey to the NNS. The first of these two surveys (NNS) has collected data on a national sample of registered births, while the second (NFMS) has collected data on a national sample of fetal deaths. Data will also be obtained from mothers, physicians, hospitals, and associated medical sources. Among the items on environmental factors are questions on smoking, occupation of mother and father, and on exposure to radiation and certain household chemicals such as pesticides. These data will be analyzed to determine possible relationships of the environmental factors with birth abnormalities and fetal mortality.

3. National Health Interview Survey (NHIS)

The NHIS, begun in 1957, provides national data on the incidence and prevalence of diseases and the extent of disability and the use of health services of the U.S. population. An interview is conducted on a national probability sample of households by trained interviewers of the U.S. Bureau of the Census, using detailed specifications supplied by the NCHS. In addition to a repeated core set of health, socioeconomic, and demographic items, there is a rotating set of supplements on a variety of health topics. There is an agreement with NIOSH for joint exploration of the analytic potential of the occupation and industry data in the NHIS to determine possible relationships between occupational exposure and environmentally related disease. In addition, the NHIS data are being used in the analysis of photochemical oxidant data in a study by EPA to determine health effects of exposure to these air pollutants.

4. National Death Index (NDI)

The NDI is a central, computerized file of data from death certificates compiled from computer tapes obtained by NCHS from state offices of vital statistics. Beginning with deaths occurring in 1979, these tapes contain a standard set of identifying data for each decedent. The data are used in searches of the NDI to identify and locate death records filed in the state offices. In this way, the NDI enables researchers who are conducting statistical studies to determine if persons in their studies may have died. If so, the Index provides the names of the states where the deaths occurred, the corresponding death certificate numbers, and the dates of death. The NDI user can then make the necessary arrangements with the appropriate state offices to procure copies of death certificates or specific statistical information such as cause of death.

Recent Advances and Research Findings

Of the specific data collection activities described above, there are a few published research findings available. Two recent reports from NHANES describe data on blood lead levels and on blood carbon monoxide levels* indicating the distribution of these pollutants in the U.S. population. Some of the findings for blood lead levels include:

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* NCHS advance data reports

1. An estimated 4.0 percent (about 675,000) of U.S. children under 6 years of age were found with elevated blood lead levels (30 micrograms or more per deciliter of whole blood).
2. Percent of children with elevated blood lead levels is much higher among black (12.2 percent) than among white (2.0 percent) children.
3. Almost one-fifth (18.5 percent) of black children from low-income families have elevated blood lead levels.
4. Among children under 6 years of age, mean blood levels are significantly higher among low income families and in larger cities (one million or more population).
5. Among children ages 6-17 years, mean blood lead levels decrease by age until about adolescence.
6. Among adults, the mean blood lead levels of men substantially exceed those of women for all the age groups.
7. Declines in mean blood levels during the period of this survey (1976-80) amounted to 30 percent or more in all age groups for both sexes and both black and white groups.

Some of the findings for blood carbon monoxide levels include:

1. The greatest source of exposure to carbon monoxide is cigarette smoking. The mean carboxyhemoglobin (COHb) level for smokers was found to be more than four times the level for those who never smoked.
2. Exposure to carbon monoxide among children ages 3-11 years was highest for those in low-income families and lowest for higher-income families. This was attributed primarily to differences in indoor sources of carbon monoxide.

3. For adults, differences in blood carbon monoxide levels by income group were not statistically significant.

4. Among children ages 3-11 years, the mean blood carbon monoxide levels were higher for those in large cities than for those in smaller cities and rural areas.

5. Black adults were found to have consistently higher blood carbon monoxide levels than white adults, which may be due in part to a greater likelihood of occupational exposure to CO among black adults.

6. Seasonal effects on concentration of blood carbon monoxide levels were evident in that values during winter months were higher. This may be due in part to indoor sources of CO such as gas stoves, furnaces, unvented space heaters and other such appliances.

Research Priorities

Within the NCHS, relative priorities for research into the possible linkage between environmental factors and human disease are determined by the legislative mandates and by the amount of funds and staff available.

The Public Health Service Act specifies, among other activities in Section 304, that the "impact of the environment on individual health and on health care" shall be given "appropriate emphasis" through research, demonstrations, evaluations, and statistical and epidemiological means. Also, within Section 306 of this Act, the NCHS is required to collect statistics on, among other items, "environmental, social, and other health hazards."

Three activities relating to environmental data required by the PHS Act have previously been completed. These are:

1. Development of a plan for collection and coordination of statistical and epidemiological data on the effects of the environment on health--in Section 306 (1)(1)

2. "Conduct a study of the issues and recommendations for establishing a Federal system to assist, in a manner designed to avoid invasion of personal privacy, Federal, State, and other entities in locating individuals who have been or may have been exposed to hazardous substances to determine the effect on their health of such exposure and to assist them in obtaining appropriate medical care and treatment"--in Section 306 (1)(3)

3. The Secretary, with the assistance of the Institute of Medicine and in cooperation with other Agencies of the Federal government (EPA, DOL, CPSC, CEA, CWPS, CEQ), shall conduct an ongoing study of present and future projected health costs of pollution and other environmental conditions resulting from human activity--in Section 304(d).

To the extent possible, these above environmental data activities were given the highest relative priority so that they could be accomplished within the time allotted.

CENTERS FOR DISEASE CONTROL

Part of CDC's mission in disease prevention and health promotion centers on the occurrence of chronic diseases in the general population. CDC conducts a variety of research and preventive activities relevant to the concerns of the Task Force on Environmental Cancer and Heart and Lung Disease. This work is particularly focused within the Chronic Diseases Division of CDC's Center for Environmental Health (CEH).

The Cancer Branch in the Chronic Diseases Division carries out projects ranging from field investigations of cancer case clusters or multiple case cancer families to long-term case control or cohort studies that frequently involve collaboration with universities and various state and/or Federal Agencies. Past work has included interpersonal contact as a risk factor in leukemia/lymphoma, studies of risk factors associated with animal tumor viruses, and epidemiologic studies of toxic chemicals and hazardous wastes as potential carcinogens. Recent field investigations have focused on populations exposed to radionuclides (e.g., plutonium, thorium, industrial facilities, and natural sources) and followup evaluations of populations with health complaints who also live near nuclear facilities.

The Special Studies Branch in the Chronic Diseases Division investigates outbreaks of disease and health risks related to manmade chemical or physical agents and to natural environmental hazards. Recent activities have involved studies of health effects of toxic agents including heavy metals, pesticides, polybrominated biphenyls, polychlorinated biphenyls, and complex mixtures arising from toxic waste disposal. Members of the Branch work closely with other parts of CDC in studies of Kaposi's sarcoma and possible precursor lesions. Other studies have been directed at respiratory and other health effects secondary to indoor air pollution.

The Birth Defects Branch in the Chronic Diseases Division has the lead role in CDC to examine the environmental causes of low birth weight, infant mortality, and chronic disabling conditions of childhood. Recent investigations have included study of clusters of congenital heart defects in Ohio and Maine. The Branch maintains a partial ongoing national registry of birth defects diagnosed in newborn children in the United States.

Research Priorities

Priorities at CEH presently focus on assistance to State and local health jurisdictions in responding to specific environmental health problems as they arise. Recent CDC involvement in such problems has included:

- Studies of respiratory illness related to indoor air pollution exposures such as formaldehyde
- Detection of high levels of DDT and PCB in the population of Triana, Alabama, with subsequent studies of that population regarding possible biologic effects
- Identification of high levels of pentachlorophenol in people living in log homes
- Study of a new toxic illness in Spain associated with ingestion of an unlabeled cooking oil causing a major epidemic of disease in that country; investigations are continuing in an attempt to identify the specific toxic agents causing this illness
- Identification of exposures to asbestos in a trailer park in Globe, Arizona, located on the site of an abandoned asbestos manufacturing plant
- Study of clusters of leukemia and kidney cancer near abandoned dump sites in Woburn, Massachusetts
- Chromosomal studies in the population potentially exposed to waste chemicals at Love Canal, New York.

A further high priority area within CEH relates to the Comprehensive Environmental Response, Compensation and Liability Act (Superfund) bill, which mandates EPA to clean up abandoned hazardous chemical waste sites and HHS (specifically CDC) to provide assistance to EPA in documenting human exposure and adverse health effects in populations near waste sites. As part of this mandate, CEH has looked at those counties that contain the first 115 sites designated by EPA for cleanup to determine if there is evidence of excess cancer in those communities that could possibly be related to exposures from those dumpsites.

FOOD AND DRUG ADMINISTRATION

The mission of the Food and Drug Administration (FDA) is to ensure that foods are safe and wholesome; that drugs, biologic products, diagnostic products, and therapeutic devices are safe and effective; that cosmetics are safe; and that use of household and medical devices emitting radiation does not result in unnecessary human exposure to radiation.

Most of the regulatory activities of the FDA are based on science and require information that derives from scientific research. Regulatory science in FDA has many aspects. In its own laboratories and through contract, FDA studies the biological effects of chemicals and radiation in order to determine hazards. The information thus obtained is used to set standards and to prepare regulations. To improve enforcement of standards and regulations, the FDA is also constantly refining its testing methods and conducting research to improve them.

Research in the FDA is conducted by the five bureaus (the Bureau of Drugs and Biologics, the Bureau of Foods, the Bureau of Veterinary Medicine, the Bureau of Radiological Health, and the Bureau of Medical Devices), by the National Center for Toxicological Research, and the regional laboratories of the Executive Director, Regional Operations.

FDA research activities that pertain to the relation between environmental factors and cancer and heart and lung disease are summarized below for each of the involved Bureaus.

The Bureau of Drugs and Biologics conducts or supports:

- Research on the toxic effects and on the mechanisms of toxicity of selected drugs
- Epidemiology research on the long-term effects of drugs used chronically
- Surveillance of drug usage to identify and analyze any relations between drug use and disease experience in children
- Research into the toxicological properties and the long-term adverse health effects of plastics and plastic components used to collect and store blood and blood products (in vitro techniques).

The Bureau of Food conducts or supports:

- Research to develop multiresidue and single residue analytical methods for pesticides, dioxins, and other industrial chemicals
- Research to develop multielement and single element analytical methods for toxic elements and methods for the determination of the chemical forms of toxic elements present in foods
- Research to develop analytical methods for the detection of mycotoxins, plant toxins, and seafood toxins in foods
- Research to develop analytical methods for detection and measurement of food additives
- Research to develop methods that measure the toxic properties of food additives and contaminants especially related to diseases, such as carcinogenesis, with long latency periods.

The Bureau of Veterinary Medicine conducts or supports:

- Research into the pathophysiological properties of environmental and natural toxins in animal feeds including interactions between such toxins and dose-response relationships

- Research to develop a cardiovascular toxicity model for the evaluation of the effects of ionoforic substances (antibiotics)
- Research into the potential for contamination with nitrosamines of foods derived from animals fed nitrosatable drugs
- Research into the kinetics, metabolism, and toxicity of industrial chemicals accidentally introduced into the feed of food animals
- Research to develop multiresidue analytical methods for animal drug residues in human food
- Research into the effects, including carcinogenesis, of long-term, low-level exposures to animal drug residues.

The Bureau of Radiological Health conducts or supports:

- Experimental and epidemiology studies of the biological effects of ionizing radiation
- Epidemiology studies designed to assess the risk of thyroid cancer following exposure to diagnostic iodine-131 in young adults
- Research into the interactions, including photocarcinogenesis, between ultraviolet irradiation from general illumination sources and chemicals, drugs, cosmetics, and food additives
- Experimental and epidemiology research into the biological effects of therapeutic and diagnostic ultrasound to quantify the possible risk associated with fetal exposures to ultrasound
- Experimental and epidemiology research into the biological effects of exposures to radiofrequency and microwave radiations.

National Center for Toxicological Research

The major emphasis of the NCTR program is to provide basic research support to the FDA and other government agencies focusing attention on critical problems in toxicology, so that regulatory actions can be based upon sound scientific evidence. To implement this program, the NCTR effort is concentrated into four mission areas: chemical evaluation, test/methods development, basic research activities, and extrapolation.

The chemical evaluation mission determines dose-response toxic effects in multiple organs/tissues, carcinogenic potential of selected chemicals, effects of diet/nutrition/environmental factors on chemical carcinogenesis, and the comparative toxic effects of hormones in susceptible and nonsusceptible strains of mice.

The methods development research areas have instituted programs to: assess genetic or specific target tissue damage following prenatal or postnatal chemical exposure; implement more efficient in vivo toxicity assays utilizing mice with specific mutation and gene patterns that increase sensitivity to various chemical classes; develop more reliable and economic in vitro methods for predicting the genotoxic potential of chemical agents; evaluate current teratology testing methods and implement new or improved procedures; investigate new procedures for the quantitation, analysis, and separating of toxic chemicals and provide sensitive methods for elucidating chemical structure; and refine assays for the evaluation of toxic agents on the immune system.

The basic research mission of the NCTR applies a mechanistic, rather than a descriptive, approach to toxicology seeking answers to explain how toxic chemicals produce cellular injury or induce toxic changes in cells. Such research includes, but is not restricted to: the role of DNA damage and repair in chemically-induced degenerative disease processes as a function of animal age and species and target organ susceptibility; understanding the synergistic interaction between physical particles and chemical carcinogens; elucidation of the metabolic pathways leading to activation and detoxification of potential carcinogens; identification of the nature of chemical damage to cellular constituents; and exploration of the biochemical pathways leading to the initiation and progression of neoplastic cells. Understanding the biological and biochemical mechanisms of cellular injury leading to impaired cellular functions, cell death, or to neoplasia, may result in the development of new techniques for prevention of disease at the subcellular level.

The combined efforts of the NCTR mission outlined above provide a data base for regulatory action and for the fourth mission of the NCTR (extrapolation) using the data from basic research and from animal models for the evaluation of potential human health risks of environmental contaminants.

Some of the current research activities in the NCTR program include:

- The design of protocols for evaluation of the carcinogenic potential of chemical compounds.
- Determination of the health effects in animals from long-term, low-level exposure to chemicals and definition of the biological processes leading to pathological responses.
- Examination of the relationship between diet/nutrition and carcinogenesis using semipurified and natural diets in chronic feeding studies with chemical carcinogens.
- Development of animal strains with gene patterns controlling particular metabolic pathways, thus increasing or decreasing sensitivity to various classes of toxic agents and providing in vivo models that are more efficient and perhaps more relevant for hazard and risk assessment.
- Detection and determination of common endpoints in DNA damage in different species, organs or tissues after exposure to toxic agents in order to extrapolate data for human risk assessment from animal models.

- Definition of the metabolic pathways in vivo that convert chemicals into active carcinogens that bind to cellular macromolecules and the influence of physiological factors and chemical structure on metabolism, binding, and carcinogenesis.

- Study of bladder carcinogenesis by arylamines including adduct formation, effect of chemical structure, influence of pH, and activation by bladder epithelium. Synergistic or cocarcinogenic effects of arylamines in the induction of local tumors is also under study.

- Studies on the effects of toxic chemicals administered transplacentally including chromosomal effects and target organ specificity. Differences in specific adduct induction, repair of induced adducts, and cellular proliferation are being studied as determinants of organ specificity.

- Experiments to evaluate the interrelationship between DNA damage, repair, and replication as a function of fetal and adult development and the susceptibility or sensitivity to tumor induction.

- Comparison of excision-repair between species or differing life spans, in an attempt to elucidate the different oncogenic responses to carcinogens manifest by different species of varying longevities and the relevance of these differences to extrapolation from animal data to human risk assessment.

- Validation and improvement of in vivo germ cell assays and in vitro mutation assays to assess chemically-induced damage in both germ and somatic cells. Heritable translocation assays that may provide dose/response data to estimate genetic risk to future generations from chemical exposure are being evaluated.

- The effect of environmental pollutants on cells from various organs as determined by binding to macromolecules, formation of specific adducts, DNA repair, DNA strand breakage, frequency of sister chromatid exchanges, and chromosomal aberrations.

- Study of induced hypertension following prenatal exposure to chemicals and the monitoring of possible associated changes in renal and vascular structure or function.

- Determination of the promoting activity of hormones in newborn and adult animals using liver and vaginal cancer as endpoints.
- Development of analytical methods to separate and detect trace levels of toxic chemicals in environmental samples.
- Refinement of analytical techniques to accurately determine concentration levels of chemicals in animal feed used for carcinogen bioassays.
- Development of cost effective methods to detect presence of toxic agents in wastewater treatment systems.

Some significant findings include:

- In carcinogen risk assessment, the NCTR ED_{01} study was designed to estimate the effective dosage of a carcinogen required to produce a 1% tumor incidence. Other objectives of the study were designed to: investigate the progression of tumors, determine the time necessary for tumor occurrence, and determine the effect of removal of carcinogen from the diet on the progression or regression of the chemical effects. Additionally, data from the study will be useful in developing reliable and more economical animal bioassays for carcinogens and in providing information for evaluation of human risk from low levels of carcinogen exposure. The study led to several important conclusions:

  --The same chemical (2-AAF) resulted in bladder and liver tumors with two distinct dose response curves. Bladder tumor incidence exhibited a minimum effect level (a nonlinear response) whereas liver tumor incidence displayed a linear dose response relationship extrapolating to zero dose.

  --Exposure time was an important factor. As the exposure to chemical was continued, tumors developed at increasingly lower doses.

  --Induction of bladder tumors was dependent upon continued exposure. Bladder tumors appeared earlier than liver tumors, but the latter occurred without continued dosing. Therefore, carcinogen bioassays must consider not only the dosage, but the time to tumor appearance in the experimental design.

- Elucidation of the metabolic pathways of arylamines involved in the induction of urinary bladder cancer. Experiments have shown that the ultimate carcinogen is formed in acidic urine. Insensitivity of the standard animal test systems (mice, rats) may be due to the higher pH of the urine as opposed to the more acidic pH of sensitive species (dogs, monkeys, humans).

- Adaptation of microencapsulation systems for the even distribution of labile, nondispersible or volatile test chemicals in animal feed for toxicological evaluations.

- Demonstration of conversion of azo dyes by intestinal microflora into compounds known to be carcinogenic to experimental animals.

- Developed analytical methodology for the determination of trace levels of dioxins (2,3,7,8-TCDD and isomeric analogs) at the 5 parts per trillion level. The methodology has been used to help define the regulatory criteria for analysis of environmental or commercial samples for 2,3,7,8-TCDD. The techniques can be applied to incinerator emissions or to distribution in dosed animals.

- Development of methods to quantitate DNA damage in vivo in dividing and nondividing cell populations. These procedures combine the rapid and economic features of prescreening with the various influential physiological factors inherent in in vivo systems.

- Completed nine subchronic (90 day) studies for evaluation of chemical toxicity with two additional compounds to be completed this year. Chronic studies (2-year) for carcinogenic effects will be performed on ten of the chemicals evaluated in the subchronic studies.

- Developed an automated data system (Toxicological Data Management System or TDMS) that provides an integrated system to assemble data generated by chronic studies including animal breeding, diet preparation, chemical surveillance, microbiological surveillance, and pathology evaluations.

- Designed and constructed a wastewater treatment plant specifically for removal of toxic materials from the industrial waste system of the NCTR facility. In conjunction with the above, a cost effective "marker" technique was developed to monitor the efficacy of the system.

- Established interagency agreements with NIOSH, CPSC, NIEHS, and USDA to conduct laboratory investigations in the areas of carcinogen metabolism, acute toxicity, data collection, in vitro bioassays, and teratology.

- Established a major cooperative program with the EPA to define the parameters controlling the effective and efficient incineration of toxic wastes. A newly constructed pilot plant at NCTR will evaluate flow rates, chamber temperature, release rates, and chemical analysis of stack emission and incinerated residue.

- Coordinated three consensus workshops or conferences concerned with: (1) In Vitro Effects of Mineral Dusts, (2) Evaluation of the ED_{01} Study, and (3) In Vitro Teratogenesis Testing. A consensus workshop on formaldehyde is scheduled for the spring of 1983. Participants for the workshops are drawn from government, industry, academia and public interest groups, to discuss and generally agree upon the scientific issues surrounding toxicological problems of major economic, sociologic, or scientific importance.

NCTR current research priorities include:

- Refinement of the chemical evaluation system with regard to responsiveness, quality control over all aspects of the studies, cost effectiveness, and data management and analysis. To fully address all toxicological issues in a chronic study, a Comprehensive Biological Assessment Program will be instituted with input from all affected research groups. This approach will provide a coordinated effort in the safety assessment of a test compound.

- Development and extension of methods to quantitatively measure DNA damage and repair in vivo. Included will be: studies on the persistence of damage, measurement of the numbers and types of distortions in DNA, effects in target and nontarget organs and tissues, relationship of damage and repair in utero to teratogenic effects, comparisons between different species under different physiological conditions, relationship to carcinogenesis/mutagenesis, effect on organ function, and relationship of repair proficiency to individual life-span.

- Development of biochemical markers to measure the progression of carcinogenesis from initiation to appearance of tumors. Included will be the biochemical events involved in cocarcinogenesis and promotion at frequent sites of human cancer (lung, breast, bowel and bladder).

- Improvement of methods to assess the toxic and immunotoxic potential of environmental contaminants. Particular attention will be given to assays measuring damage to functional cells and germ cells, and to techniques that demonstrate the effects of toxic agents on immune competence.

- Determination of nutritional/diet/hormonal factors that increase or decrease an animal's response to toxic chemicals, particularly organ function and carcinogenesis employing semipurified and natural diets.

Chapter 6

STATUS OF TASK FORCE ACTIVITIES

The Task Force began its fifth year with the active participation of a new Chairperson, Dr. John W. Hernandez, Jr., Deputy Administrator of EPA. The Task Force Working Group, composed of representatives from the eight Agencies, reassessed its directions in terms of the mandate contained in Section 402(b) of Public Law 95-95. The Working Group decided to undertake activities to specifically address first the mandate in Section 402(b)(1), the recommendation of a comprehensive research program to determine and quantify the relationship between environmental pollution and human cancer and heart and lung disease. To implement Section 402(b)(1), the Task Force seeks to answer the following questions:

1. What is known about the possible link between environmental pollution and human cancer and heart and lung disease?
2. What information is missing that, if obtained, is likely to clarify the nature and strength of such a link?
3. What are the current and feasible research activities that could conceivably yield such information?

In light of these questions, the Task Force refocused some of the information acquired through past activities, redirected some of its ongoing activities, and initiated new activities. These changes were reflected in the efforts of the Working Group and its Project Groups.

WORKING GROUP

The Task Force Working Group is made up of representatives designated by the member Agency Directors. Dr. Hernandez, Chairperson of the Task Force, appointed Dr. Maria Pavlova, of the Office of Research and Development, Chairperson of the Working Group. By establishing objectives, deciding on activities, reviewing outcomes, and sharing their technical expertise, the Working Group provides the dynamic momentum of the Task Force as it acts to address its mandates.

Workshops

The Task Force Working Group considered several options that might be undertaken to answer questions about the relationship between the environment and human disease. The Working Group decided that the holding of workshops would be an effective means of obtaining such information. Scientists in the Federal Government, academia, and industry will meet to summarize what is known about the link between the environment and disease and recommend what research should be done to extend our knowledge.

After a preliminary information-gathering exercise and discussion of possible topics, in May 1982 the Task Force formally decided to sponsor a workshop on environmentally related nononcogenic lung diseases. While much attention has been focused on lung cancer, relatively little is known about the nononcogenic lung diseases. The present state of knowledge in this area will be described as a prelude to identifying future research needs.

Generic research needs, rather than those identified with specific pollutants, will be emphasized. The emphasis will be on air pollution with the lung as target, but other media and organ systems will not be excluded, particularly if the lung is the portal of entry.

The workshop, expected to last for two to three days, is tentatively scheduled for late winter, 1983. It is anticipated that participants will make short presentations to provide the background for topics under discussion. The presentations will be in the broad subject areas of basic and animal research, clinical studies, and epidemiology and health data banks. The proceedings of the workshop will be published.

The Task Force considers that such a workshop can effectively summarize what is known about the link between environmental pollution and human disease. The overview of human adverse effects thought to be associated with environmental pollution can point toward what needs to be known about disease etiologies and mechanisms.

Information Exchange

As an interagency group, the Task Force is a stimulus to the exchange of information among Federal Agencies. This exchange of information is a prerequisite to responding to the Task Force mandate to "coordinate research by, and stimulate cooperation between, the Environmental Protection Agency, the Department of Health, Education, and Welfare (now the Department of Health and Human Services) and such other Agencies as may be appropriate to prevent environment-related cancer and heart and lung disease" (P.L. 95-95, Section 402(b)(4)). Since its inception, the Task Force has conducted various information exchange activities. During its fifth year, the major information exchange activities were

- Publication of the third edition of the Directory of Federal Interagency Groups Concerned with Environmental Health
- Collection and summarizing of relevant reports and recommendations from Federal Agencies, interagency groups, and the scientific literature.

The third edition of the Directory was published in December 1981 and reflects extensive changes that have been made in the memberships and the mandates of many of the groups. The Directory presents information on the membership, charter, activities/accomplishments, publications, products, meeting schedule, and duration of 20 groups and 7 subgroups. An index of representatives provides telephone numbers for all persons who are listed as members of the groups. The Directory is a valuable resource for persons in and outside of government who are interested in the relationship of environmental factors to human health. Information about these interagency groups is helpful in analyzing Federal research activities on environment-related disease.

The Task Force continued to monitor and collect reports from Federal Agencies, interagency groups, and the scientific literature that are relevant to Task Force interests. Appendix D contains an annotated listing of some of the recent reports identified. By maintaining awareness of current research activities, the Task Force can focus its own work to avoid duplication of effort or apportion emphasis, as appropriate.

Project Inventory

As one of its fourth-year activities, the Task Force compiled and classified research projects and other activities in the area of environment-related disease that were supported in FY80 by its member Agencies. Approximately 4,000 projects are included in the inventory and classified by type of activity, disease endpoint, and sponsoring division within each Agency. More than 85 percent of the projects included are research projects, with the remainder in the areas of education and preventive medicine.

During its fifth year, the Task Force designed a preliminary analysis of the vast amount of data to identify those areas in which research was being emphasized or was lacking. The draft Project Inventory Analysis, published in January 1982, included graphical presentations of Project Inventory classifications and various types of summarizations of Inventory information. When the Working Group looked at the Inventory from this level of detail, the intended analysis was compromised by the inconsistency of data contained in project abstracts. For a successful inventory of research, it is necessary that the Agencies have a standard consistent method of reporting information on their research activities. Comparisons and analyses cannot be made without similar data elements. As described below, the Task Force decided that identification of research gaps and overlaps could best be accomplished by the development of a mechanism to bring together Agency planning personnel.

Research Coordination

With each meeting of representatives from the eight Agencies, the Task Force responds to the mandate contained in Section 402(b)(4), to coordinate research by and stimulate cooperation among the Agencies. During its fifth year, the Task Force began to investigate the development of a mechanism for the exchange of information output emanating from Agency research programs and changes in these programs. It was suggested that research projects be grouped by areas defined by intramural personnel. The Task Force will attempt to provide the mechanism that would enable those responsible for health research planning in any one Agency to interact with their counterparts in other Agencies.

PROJECT GROUPS

The Task Force Project Groups are subgroups of interagency representatives, established by the Working Group to focus on specific problem areas in the study of environment and disease. During this fifth year of the Task Force, the Project Groups have continued ongoing activities, finished past efforts, and moved on in new directions. The specific activities of the Project Groups are described below.

Project Group on Exposure and Metabolic Mechanisms

Under the continuing direction of Dr. Morris Kelsey of the National Cancer Institute, the Project Group continued to document and build on the information derived from its January 1981 Workshop on Exposure to Environmental Agents, Their Metabolism and Mechanisms of Toxicity. The document summarizing the research needs and their accompanying rationales was published and submitted to Congress with the Task Force's Fourth Annual Report on August 7, 1981. The Workshop report was referenced in several scientific publications and has been widely disseminated in response to requests from persons in Federal Agencies, state health departments or environmental protection offices, medical schools, universities, associations, public and private organizations, and industry. In several instances, multiple copies were requested for Agency planning staffs, boards of directors, and libraries. Copies of the report are still available for distribution.

To further document the Workshop, the position papers that provided the basis for Workshop discussion were published in a special issue of the Journal of Environmental Science and Health (Volume 17A, Issue 4, July 1982). Workshop participants were contacted, and 20 papers were collected and prepared for publication. The position papers focus on approaches to the problem of environmentally related disease from a multidisciplinary standpoint. This special journal issue offers a unique contribution because the papers are not scientific papers in the usual sense of reports of scientific investigations. Rather, each paper is a synthesis of scientific thinking and innovative concepts derived from the author's total scientific experience.

In another effort to develop and highlight some of the Workshop's recommendations and identify gaps in knowledge, the Project Group engendered two working groups. One subcommittee, headed by Dr. James Gillette from NHLBI, is focusing on metabolism. Their objective is to study the problems associated with the extrapolation of metabolic mechanisms observed in animal or in vitro studies to those expected or observed in humans. The group is expanding and modifying some of the relevant Workshop recommendations into a document that will describe strategies needed for extrapolation of animal data to humans.

The other subcommittee, led by Dr. Thomas Mason of NCI, was formed to address the problems involved in obtaining exposure data for epidemiology studies. This group is also reviewing the 1981 Workshop recommendations to assess their completeness and will develop a hierarchical list of implementable research recommendations for assessing exposure. Reports from both subcommittees will be submitted to the Working Group during the next year.

As an adjunct to this activity, the subgroup is also involved in the planning and sponsorship, with Dr. Constantine Zervos of the FDA Scientific Liaison Staff, of a conference entitled "Exposure Assessment: Problems and Prospects." The conference will be held on the NIH campus on September 13 and 14, 1982. The framework of the conference encompasses three disease endpoints--lung cancer, colon cancer, and birth defects--and the various methodological problems involved in assessing exposures that might contribute to these diseases.

Project Group on Standardization of Measurements and Tests

An essential element of any "...research program to determine and quantify the relationship between environmental pollution and human cancer and heart and lung disease" (P.L. 95-95, Section 402(b)(1)) is consistent, high-quality measurement of environmental pollution levels and human exposures. These measurements are based on samples from environmental media and human tissues and body fluids. Under the direction of Dr. Robert Medz of EPA, the Project Group undertook a feasibility study to test the hypothesis that laboratory data quality is positively related to the share of analytical workload that is devoted to quality control samples. It was theorized that if such a relationship could be quantified, it could be used to develop a program planning tool for allocating laboratory resources to achieve optimal data quality.

The Project Group studied the relationship of data quality levels to control sample frequencies for 12 state and university laboratories that participated in 1978 and 1979 in an Epidemiological Studies Program (ESP), administered by the EPA Office of Pesticide Programs. General, substrate-specific and pesticide-specific analyses were conducted. The major conclusions of the study were

- There was no systematic relationship between data quality and frequency of quality control analyses; or
- The feasibility study data base has deficiencies that prevent the relationship from being detected.

The Project Group presented the final report of the feasibility study to the Working Group in January 1982.

At the March 3, 1982, Working Group meeting, Dr. Medz stated that because of the Agencies' different interests, it is not practical to standardize methods across Agencies. While emphasizing the importance of quality assurance/quality control activities, he asked the Working Group to phase out the Project Group. The Working Group concurred with Dr. Medz's request, and the Project Group was officially disestablished.

Project Group on Quality Assurance in Analytical Methodology

To implement the Task Force decision to establish a new project group in the area of quality assurance, the following objectives were submitted for Working Group approval at the May 27, 1982, meeting:

- Promote and foster interagency cooperation in the development of analytical methodology to monitor the environment for manmade and natural toxins
- Determine whether the Agency quality assurance programs for regulatory analytical methods reflect high standards
- Reconcile by consensus any divergent views among the regulatory Agencies on particular regulatory methods that are important to the protection of public health and the environment.

Once the objectives are agreed upon and participants have been selected the group will meet to develop specific approaches to the first two objectives above.

Project Group on Education of the Public and of Health Professionals

An informed public may be the most effective strategy for reducing costs and risks associated with environmentally related cancer, heart, and lung diseases. This project group, chaired by Dr. George Simon of EPA, directed its attention this year toward the education of the public. A study was made to identify available resources, and to identify material currently being disseminated through various media concerning environmental pollution and disease.

It was determined that a large number of resources and a large amount of information regarding environmentally related diseases are available for use in the education of the public. These resources include various Federal, state, and professional organizations as well as industrial organizations. However, the dissemination of this material has been very limited and/or restricted to certain defined populations. There appears to have been no coordinated, concerted effort to provide the public with the information that is available.

The Project Group recommended that future efforts should be to investigate strategies and methods for the dissemination, to the public, of the available information on health effects caused by environmental pollutants. Results of the proposed lung disease workshop sponsored by the Task Force, and results from the proposed work of the Interagency Education Program Liaison Group on a clearinghouse program may significantly contribute to this activity.

Interagency Education Program Liaison Group

The IEPLG, established as a result of a recommendation in the Task Force's Third Annual Report, is to coordinate and stimulate Federal activities in the area of environmental and occupational health professional education. Chaired by Dr. Max Lum of HRSA, with Dr. Wilford Nusser of NIEHS as the principal scientist, the IEPLG conducted a feasibility study to determine the need, potential uses of, and resource requirements necessary to establish an educational resource center for environmental and occupational health professionals. The survey of non-Federal respondents disclosed significant support for such a center.

Therefore, with the approval of the Working Group, the IEPLG began to acquire, assemble, and organize educational materials for health professionals. The materials are related to the prevention, diagnosis, treatment, or limitation of environmentally related disease. This collection effort will culminate in the assembly of a Federal review panel that will inventory and report on environmental/occupational educational programs within their Agencies' statutory authority. An annotated bibliography of currently available materials and a summary of the workshop proceedings will be prepared.

The IEPLG also plans to organize a panel of medical educators and persons representing a cross-section of professional organizations, academic medical centers, teaching hospitals, and practicing physicians. The IEPLG will then synthesize the information from both panels and prepare an assessment report summarizing findings and recommendations relevant to gaps and needs and techniques and approaches to develop and disseminate educational materials for use by health educators and practitioners. The anticipated goal of this effort will be to provide health practitioners with information to maximize the use of existing health educational resources and help Federal policymakers make decisions about future educational resource needs.

Appendix A

PERTINENT SECTION OF PUBLIC LAW 95-95

PUBLIC LAW 95-95

Clean Air Act Amendments of 1977

"INTERAGENCY COOPERATION ON PREVENTION OF ENVIRONMENTAL CANCER AND HEART AND LUNG DISEASE

Sec. 402. (a) Not later than three months after the date of enactment of this section, there shall be established a Task Force on Environmental Cancer and Heart and Lung Disease (hereinafter referred to as the 'Task Force'). The Task Force shall include representatives of the Environmental Protection Agency, the National Cancer Institute, the National Heart, Lung, and Blood Institute, the National Institute [for] Occupational Safety and Health, and the National Institute [of] Environmental Health Sciences, and shall be chaired by the Administrator (or his delegate).

(b) The Task Force shall--

(1) recommend a comprehensive research program to determine and quantify the relationship between environmental pollution and human cancer and heart and lung disease;

(2) recommend comprehensive strategies to reduce or eliminate the risks of cancer or such other diseases associated with environmental pollution;

(3) recommend research and such other measures as may be appropriate to prevent or reduce the incidence of environmentally related cancer and heart and lung diseases;

(4) coordinate research by, and stimulate cooperation between, the Environmental Protection Agency, the Department of Health, Education, and Welfare, and such other agencies as may be appropriate to prevent environmentally related cancer and heart and lung diseases; and

(5) report to Congress, not later than one year after the date of enactment of this section and annually thereafter, on the problems and progress in carrying out this section."

Appendix B

MEMBERS OF THE TASK FORCE, WORKING GROUP, AND PROJECT GROUPS

TASK FORCE PLENARY

EPA	John W. Hernandez, Jr., Deputy Administrator Maria Pavlova, Office of Research and Development	Chairperson Working Group Chairperson
NCI	Vincent T. DeVita, Director Herman F. Kraybill, Scientific Coordinator for Environmental Cancer, Division of Cancer Cause and Prevention	
NHLBI	Claude J.M. Lenfant, Director Suzanne S. Hurd, Acting Director, Division of Lung Diseases Manning Feinleib, Associate Director for Epidemiology and Biometry, Division of Heart and Vascular Diseases	
CDC	William H. Foege, Director Clark W. Heath, Jr., Director, Program Development Office, Office of the Director	
CDC: NIOSH	J. Donald Millar, Director Kenneth Bridbord, Director, Office of Extramural Coordination and Special Projects	
NIEHS	David P. Rall, Director Raymond E. Shapiro, Assistant Director for Toxicology Coordination	
NCHS	Robert A. Israel, Acting Director Rosalie A. Dunn, Epidemiology Branch, Office of Analysis and Epidemiology Sam C. Marcus, Special Assistant to the Director	
FDA	Arthur H. Hayes, Jr., Commissioner Constantine Zervos, Director, Scientific Liaison Staff	

WORKING GROUP

EPA	Maria Pavlova, Office of Research and Development	Chairperson
	George R. Simon, Science Review Administrator for Health Research, Office of Research and Development	
NCI	Herman F. Kraybill, Scientific Coordinator for Environmental Cancer, Division of Cancer Cause and Prevention	
	Morris I. Kelsey, Assistant to the Scientific Coordinator, Division of Cancer Cause and Prevention	
NIEHS	Wilford L. Nusser, Associate Director for Extramural Programs	
	Raymond E. Shapiro, Assistant Director for Toxicology Coordination	
HRSA	Max Lum, Medical Education Specialist, Division of Medicine, Bureau of Health Professions	
CDC	Clark W. Heath, Jr., Director, Program Development Office, Office of the Director	
	George Hardy, Assistant Director, Washington Office	
CDC: NIOSH	Kenneth Bridbord, Director, Office of Extramural Coordination and Special Projects	
NHLBI	Suzanne S. Hurd, Acting Director, Division of Lung Diseases	
	Hugh B. Stamper, Division of Lung Diseases, Interstitial Lung Diseases Branch	
	Manning Feinleib, Associate Director for Epidemiology and Biometry, Division of Heart and Vascular Diseases	
	A. Richey Sharrett, Medical Officer, Division of Heart and Vascular Diseases, Epidemiology Branch	
NCHS	Rosalie A. Dunn, Epidemiology Branch, Office of Analysis and Epidemiology	
	Sam C. Marcus, Special Assistant to the Director	
FDA	Constantine Zervos, Director, Scientific Liaison Staff	
	Lois Ann Beaver, Staff Science Advisor	

PROJECT GROUPS

Education of the Public and of Health Professionals

EPA	George R. Simon, Science Review Administrator for Health Research, Office of Research and Development	Chairperson
	Karen Morehouse, Program Analyst, Division of Air, Noise, and Radiation, Office of Health Research	
CDC: NIOSH	Alan D. Stevens, Director, Division of Training and Manpower Development	
	P.G. Rentos, Training Grant Program Officer, Division of Training and Manpower Development	
	Marsha Bernard, Occupational Health Nurse Educator, Division of Training and Manpower Development	
NIEHS	Wilford L. Nusser, Associate Director for Extramural Programs	
NCHS	Sam C. Marcus, Special Assistant to the Director	
NHLBI	Sydney Parker, Psychologist, Division of Lung Diseases, Prevention, Education and Manpower Branch	
DOL	Edward J. Bergin, Program Analyst, Office of the Assistant Secretary for Policy, Evaluation and Research	
OSHA	Earl D. Heath, Director, Office of Training and Education	
ED	Walter J. Bogan, Director, Office of Environmental Education	
HRSA	William J. Holland, Deputy Chief, Education Development Branch; Chief, Program Development Section, Division of Associated Health Professions, Bureau of Health Professions	
	Louis Steinberg, Chief, Educational Development Report Section, Educational Development and International Activities Branch, Division of Medicine, Bureau of Health Professions	
	Max Lum, Medical Education Specialist, Division of Medicine, Bureau of Health Professions	
	Nancy J. Story, Program Analyst, Division of Medicine, Bureau of Health Professions	

PROJECT GROUPS (Continued)

Standardization of Measurements and Tests (Disestablished March 1982)

EPA	Robert B. Medz, Senior Environmental Scientist, Water and Waste Management Division, Office of Monitoring Systems and Quality Assurance Christopher Timm, Director, Quality Assurance Management Staff	Chairperson
CDC	David D. Bayse, Director, Clinical Chemical Division, Center for Environmental Health	
CDC: NIOSH	Judd Posner, Chief, Measurement Services Section, Measurement Research Support Branch, Division of Physical Sciences and Engineering	
NIEHS	Phillip Albro, Environmental Chemistry Branch	
FDA	Lois Ann Beaver, Staff Science Advisor	

Exposure and Metabolic Mechanisms

NCI	Morris I. Kelsey, Assistant to the Scientific Coordinator, Division of Cancer Cause and Prevention Herman F. Kraybill, Scientific Coordinator for Environmental Cancer, Division of Cancer Cause and Prevention Elizabeth K. Weisburger, Assistant Director for Chemical Carcinogenesis, Division of Cancer Cause and Prevention Thomas J. Mason, Chief, Population Study Section, Environmental Epidemiology Branch	Chairperson
FDA	Ronald W. Hart, Director, National Center for Toxicological Research	
CDC	Jean French, Health Scientist, Chronic Disease Division, Center for Environmental Health Clark W. Heath, Jr., Director, Program Development Office, Office of the Director	

PROJECT GROUPS (Continued)

Exposure and Metabolic Mechanisms (Concluded)

CDC: NIOSH	Richard W. Niemeier, Section Chief, Acute and Subchronic Toxicology, Division of Biomedical and Behavioral Sciences	
	Harry B. Plotnick, Section Chief, Mechanics of Industrial Disease, Division of Biomedical and Behavioral Sciences	
	Pervis C. Major, Chief, Immunology Section, Division of Respiratory Disease Studies	
EPA	Lance Wallace, Environmental Scientist, Office of Monitoring Technology Support	
	Wayne M. Galbraith, Toxicologist, Office of Health Research	
NIEHS	Larry G. Hart, Assistant to the Director	
NCHS	Sam C. Marcus, Special Assistant to the Director	
NHLBI	James Gillette, Chief, Laboratory of Chemical Pharmacology	
USDA	John E. Spaulding, Director, Residue Evaluation and Surveillance Division, Food Safety and Quality Service	

Subgroup on Exposure

NCI	Thomas J. Mason, Chief, Population Study Section, Environmental Epidemiology Branch	Chairperson
	Aaron Blair, Acting Head, Occupational Studies Section, Environmental Epidemiology Branch	
	Morris I. Kelsey, Assistant to the Scientific Coordinator, Division of Cancer Cause and Prevention	
EPA	Lance Wallace, Environmental Scientist, Office of Monitoring Technology Support	
FDA	Constantine Zervos, Director, Scientific Liaison Staff	
NCHS	Rosalie A. Dunn, Epidemiology Branch, Office of Analysis and Epidemiology	

PROJECT GROUPS (Concluded)

Subgroup on Metabolism

NHLBI	James Gillette, Chief, Laboratory of Chemical Pharmacology	Chairperson
NCI	Elizabeth K. Weisburger, Assistant Director for Carcinogenesis, Division of Cancer Cause and Prevention Morris I. Kelsey, Assistant to the Scientific Coordinator, Division of Cancer Cause and Prevention	
NIEHS	Larry G. Hart, Assistant to the Director	
FDA	Constantine Zervos, Director, Scientific Liaison Staff	

Appendix C

LIST OF PUBLICATIONS ORIGINATING
FROM THE
TASK FORCE ON ENVIRONMENTAL CANCER
AND HEART AND LUNG DISEASE

Environmental Cancer and Heart and Lung Disease, Fourth Annual Report to Congress, August 7, 1981

This report describes the work of the Task Force in its fourth year and outlines plans for the future. The establishment of the Task Force and its ongoing activities are discussed in the context of the environmental disease problem. The report contains recommendations to Congress and research needs identified by a Task Force-sponsored workshop. A summary of an inventory of Agency-funded environmental health research at the project level is included.

Environmental Cancer and Heart and Lung Disease, Third Annual Report to Congress, August 7, 1980

This document presents the major activities of the Task Force during its third year and describes the initial process for developing specialized recommendations relevant to the Task Force mission. In addition to the expansion of information exchange activities (and the inclusion of FDA as the eighth member), the Task Force continued to increase its efforts in the areas of environmental health education and also risk assessment as enumerated in a separate report comparing the various criteria used by Federal Agencies to regulate carcinogens. An inventory of Agency-funded research at the program level is included.

Environmental Pollution and Cancer and Heart and Lung Diseases, Second Annual Report to Congress, August 7, 1979

In the report on second year work, the following progress was indicated and described. Project Groups were formed on Standardization of Measurements and Tests, Education of the Public and of Health Professionals, and Exposure and Metabolic Mechanisms. Information exchange among member Agencies of the Task Force was considered the primary basis for establishing coordination and development of interagency programs. Funding was identified and classified in each Task Force member Agency.

First Annual Report to Congress by the Task Force on Environmental Cancer and Heart and Lung Disease, August 7, 1978

In this first report to Congress, the Task Force summarized the problem of environmental cancer and heart and lung diseases as an interagency/interdisciplinary issue that faced the Nation as of 1978. The Task Force subsequently identified six important areas of research in which early interagency cooperation could address these issues. These research areas are: standardization of measurements and tests, exposure and metabolic mechanisms for pollutants, early indicators of disease, risk assessment, education of the public and of health professionals, and strategies to protect public health.

Summary of the Workshop on Exposure to Environmental Agents, Their Metabolism, and Mechanisms of Toxicity: Research Needs, August 1981

This report presents the full text and rationale of 72 research recommendations developed through a consensus of scientific experts at a Workshop on Exposure, Metabolism, and Mechanisms of Toxicity held in January 1981. The document is a compilation of research needs for environmental cancer and heart and lung disease in areas such as epidemiology, exposure quantification and monitoring, metabolism, and disease processes. Both short- and long-term needs are identified in a balanced focus on basic and applied environmental disease research.

Publication of Position Papers from the Workshop on Exposure to Environmental Agents, Their Metabolism, and Mechanisms of Toxicity, July 1982

Papers submitted by a selected team of scientists and used as background and reference sources for Workshop discussion were published as a special issue of the Journal of Environmental Science and Health (Volume 17A, Issue 4, July 1982). A wide range of topics included: initiation/promotion concepts of carcinogenesis, toxicologic interactions and pathogenesis of lung and heart disease, and total exposure models in animals and humans.

Project Inventory

1. Summary Report of the Project Inventory, August 1981

This document is one of three publications produced through a comprehensive survey of FY80 research projects sponsored by Task Force Agencies. The Summary Report outlines and discusses the background of the previous Inventories and summarizes the current methodology used in compiling and categorizing project information. Descriptors, including research category, subcategory, disease endpoint, and Agency division, are used in summary matrices that present totals in terms of number of projects and funding levels. This report provides a unique comprehensive picture of Task Force Agencies environmental health research efforts.

2. A Detailed Profile of Task Force Member Agency Projects in Environmental Cancer and Heart and Lung Disease, 1981

This publication presents a detailed breakdown of Agency activities and expenditures. The number of projects and dollars expended according to category and disease endpoint are shown for each Agency and division.

3. A Listing of Projects Included in the Project Inventory, 1981

This document lists all relevant research projects and includes information on project number, project title, categorization, funding level, and contact person. The data are organized by subject area and by Agency.

4. Project Inventory Analysis, Draft January 1982

This document is based on the data compiled in the 1981 Project Inventory. It includes graphical representations of Task Force Agencies' FY80 expenditures and numbers of projects in environmental disease research. In addition, research projects are summarized and previously published research recommendations are presented.

Report of the Inventory of Federal Research Programs of Relevance to the Task Force, April 1980

This initial inventory is a compilation of research program information from Task Force member Agencies in a common format for 115 research programs. Details pertaining to each research program are given to facilitate general coordination. Summary information on program description, resources applied, person-year effort, objectives and mandated responsibilities, activities, and future research and resource needs is included.

Directory of Federal Interagency Groups Concerned with Environmental Health, October 1979 and April 1980

First edition: October 1979. The document was compiled to enhance the availability of knowledge on environmental health. Information on 24 committees is included. The first edition, which is out of print, was superseded by a second edition.

Second edition: April 1980. This edition updated and expanded the information that was presented in the first edition. The second edition included information on 33 interagency committees and their subcommittees or components that deal with environmental health. Designed as a reference tool to locate interagency committees and their components, the directory is intended to promote coordination and information exchange among the listed groups and the Agencies and institutions involved in identifying problems and initiating research in environment-related cancer and heart and lung disease.

Third edition: December 1981. This edition contains revised listings of the interagency committees included in the 1980 Directory. Each listing includes names of committee representatives, the authorizing charter, relevant publications and accomplishments, and meeting schedule.

Directory of Exposure-related Data Bases, 1981

This directory provides key information on a variety of specialized exposure data bases. A description of the purpose, scope, quality of data, format, and accessibility of each data base is included.

Feasibility Plan for a Resource Center on Environmental and Occupational Health Professional Education Material, Draft September 1981

This report studies the issue of establishing a national center for the dissemination of available information on environmental health to both health professionals and the general public. Information is compiled on current and planned educational activities in the public sphere, as well as types of materials available in the medical sector.

Feasibility Study on Data Quality, January 1982

The Project Group on Standardization of Measurements and Tests developed a study on quality of data produced by chemical laboratories. Chemical measurement programs were reviewed to obtain data quality indices.

A Summary of the Legislative Framework for Risk Assessment by Task Force Agencies in the Environmental Health Context, Draft 1981

This document compares the legislative mandates under which Federal regulatory Agencies operate when dealing with carcinogens. The report presents the criteria used in judging risk, defines a health risk, and analyzes the role of costs and benefits related to risk reduction vis-a-vis regulation.

Calendar, Monthly Issue, June 1979-December 1981

The Calendar was distributed monthly to facilitate information dissemination within a 3-month time frame. The Calendar announced meetings, conferences, symposia, courses, public hearings, and workshops that pertained to environmental pollution and disease.

A Tracking Mechanism for Federal Research: Health Effects of Groundwater Sources of Drinking Water, 1981

This report delineates the stages that research recommendations undergo from inception through implementation, using groundwater quality as the topic of concern. By tracing the recommendations made in the groundwater area over the past few years, the report follows subsequent plans, research projects, and findings in an attempt to analyze how Government responds to research recommendations.

Summary of the Workshop on Environmental Education Needs of Health Professionals, December 1979

Held by the Project Group on Education of the Public and of Health Professionals, this 2-day workshop identified the needs of health professionals in environmental education. To meet these needs, the workshop participants developed action plans that were aimed at increasing health professional capabilities in effectively preventing environment-related disease. Workshop participants included representatives from health professional organizations, labor unions, and concerned Federal Agencies. The purpose of this document is to report on the activities of the Project Group before, during, and since the October 1979 workshop; to publish the methodology and summary of the workshop; and to outline the type of recommendations expected to result from the workshop output.

Recommendations on Environmental and Occupational Education of Health Professionals, Project Group on Education of the Public and of Health Professionals, Ralph E. Yodaiken, Chairman, April 1980

The recommendations that resulted from a 2-day workshop on the environmental education needs of health professionals are presented in this document. These recommendations outline a strategy through which health professionals can more effectively prevent environment-related diseases. Included in the strategy are the establishment of an Interagency Education Program Liaison Group and specific recommendations addressing curriculum, faculty, students, continuing education, and research components.

A Comparison of Scientific and Procedural Bases Used by Federal Agencies for the Regulation of Carcinogens, February 1980

This document summarizes the risk assessment activities conducted by Federal Agencies, interagency groups, scientific panels, and private groups in the field. A comparison of the scientific and procedural bases used by Federal Agencies for regulating carcinogenic substances is presented.

Report of the Project Group on Exposure and Metabolic Mechanisms, April 1980

This report synthesizes discussions, ideas, literature searches, and proposed approaches for continuing activities of the Project Group. The Group's overall efforts are directed at establishing a mechanism to achieve interagency cooperation and developing recommendations for needed research in relating exposure to environmental pollutants, their human intake, toxicity, and metabolic fate. The Project Group enumerated nine areas where empirical research should continue.

Appendix D

RECENT AGENCY AND INTERAGENCY PUBLICATIONS RELEVANT TO THE INTERESTS OF THE TASK FORCE*

Atomic Energy of Canada, Ltd.

Record Linkage: Development and Present State of the Art in Canada. AECL. November 1979. 14 pp. NTIS-AECL-6688 ($5.00).

Examines Canada's system of using computer files in conjunction with exposure data to conduct large-scale epidemiology studies.

Council on Environmental Quality

Chemical Hazards to Human Reproduction. Clement Associates, Inc. January 1981. 308 pp. NTIS-PB81-191041 ($23.00) (Tel. 703-487-4650).

Evaluates and reviews effects of exposure to chemical hazards on reproduction and policy implications of regulatory decisions.

Drinking Water and Cancer, Review of Recent Findings and Assessment of Risks. 1980. NTIS-PB81-128-167 ($11.00) (Tel. 703-487-4650).

Reviews five epidemiological studies that report increased risk of rectal, colon, and bladder cancer associated with drinking chlorinated surface water.

Environmental Quality--Eleventh Annual Report. December 1980. 500 pp. GPO-041-011-00053-0 (Tel. 301-783-3238)

Presents a comprehensive report on the status of numerous environmental issues such as ozone-layer depletion, long-range transport of air pollutants, water contamination, exposure to toxic substances, long-term energy development, natural resource protection, land use, and economic factors. Lead, caffeine, and diesel exhaust are singled out as three toxic substances to which many people are exposed and as deserving Government attention regarding the tradeoff between risks and benefits of their continued use.

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* This is a listing of some Agency and interagency reports published within the last 2 to 3 years on subjects related to the concerns of the Task Force. This listing is not the result of a comprehensive literature search and should not be construed as definitive or as constituting the endorsement of the Task Force.

Federal Interagency Committee on Health and Environmental Effects of Energy Technologies (FICHEEET)

Health Effects of Coal Technologies: Research Needs. MITRE. September 1980. 212 pp. NTIS-DOE/HHS/EPA-05 ($17.00) (Tel. 703-487-4650).

Identifies potential human health effects associated with coal mining and processing, and recommends priority research areas.

Health and Environmental Effects of Oil and Gas Technologies: Research Needs. MITRE. R. Brown. July 1981. 730 pp. MITRE #MTR-81W77 (Tel. 703-827-6217).

Presents comprehensive view of health and environmental issues related to oil and gas technology development. Includes summaries of health needs for air and water contaminants, occupational hazards, waste disposal, and offshore accidents.

Health and Environmental Effects of Synthetic Fuel Technologies: Research Priorities. MITRE. 1981. NTIS-PB81-212474 ($18.50) (Tel. 703-487-4650).

Provides assessment of potential synthetic fuel impacts on human health and discusses research needs.

Federal Trade Commission

Staff Report on the Cigarette Advertising Investigation. M. Myers. May 1981. (Tel. 202-523-3598).

First and third chapters provide review of health effects of smoking in terms of cancer, heart, and lung disease and examine consumer knowledge of health risks involved.

General Accounting Office (GAO)

Environmental Protection Issues in the 1980's. S. Madonia. December 1980. CED-81-38 (Tel. 202-275-6241).

Examines current and future issues relating to Federal participation in environmental health regulation and research.

Clean Air Act: Summary of GAO Reports (October 1977-January 1981) and Ongoing Reviews. Community and Economic Development Division. April 1981. 28 pp. ($6.50) NTIS-PB81-185662.

Reviews and evaluates variety of issues concerned with implementation of Clean Air Act.

Problems in Assessing the Cancer Risks of Low-Level Ionizing Radiation Exposure. Energy and Minerals Division. January 1981. Volume 1, 97 pp. EMD-81-1-Vol. 1, NTIS-HRP-0902935/6 ($9.50); Volume 2, 680 pp. EMD-81-1-Vol. 2, NTIS-HRP-0902936/4 ($40.00).

Analyzes the status of knowledge regarding cancer risks from low-level exposure to ionizing radiation. Recommendations for continued research are included.

Interagency Radiation Research Committee

Federal Strategy for Research into the Biological Effects of Ionizing Radiation. June 1981. NIH-81-2402 (Tel. 301-496-3152).

Includes discussion of research priorities on radiation exposures and health risks and suggested directions for future-effects research.

Research on Health Effects of Radiation, Volume 1, Parts A and B. September 1980. (Tel. 301-496-3152).

Records Federal activities in research on health effects of ionizing radiation (1978-1980) and includes a list of pertinent regulations, resolutions, and committee reports from Congress.

Joint Report to Congress by EPA and NRC

Health Effects on Low Level Ionizing Radiation. August 1979. NUREG-0602; EPA-600/8-79-019 (Tel. 703-487-4600).

Assesses the research needs and capabilities of the two Agencies in relation to their public health responsibilities.

Los Alamos Scientific Laboratory

Cancer Risks after Radiation Exposures. 1980. 18 pp. CONF-8009126-1; NTIS-LA-UR-80-3669 ($5.00).

Presents information on relationships of radiation dosage to cancer risk and lists cancer mortality percentages due to major radioactive sources.

National Academy of Sciences

Federal Research on the Biological and Health Effects of Ionizing Radiation. Committee on Federal Research on the Biological and Health Effects of Ionizing Radiation. 1981. 852 pp. (Tel. 202-389-6797).

A comprehensive inventory and analysis of 900 radiation health effects research projects supported by 15 Federal Agencies. Discusses objectives, quality, and utilization of research for planning of future research efforts.

Diet, Nutrition, and Cancer. 1982. Committee on Diet, Nutrition, and Cancer. Washington, D.C.: National Academy Press (National Academy Press, 2101 Constitution Avenue, NW., Washington, D.C. 20418)

Reviews the role of diet and nutrition in the etiology and prevention of cancer and offers interim guidelines on diet and cancer.

National Academy of Science/Insitute of Medicine

Costs of Environment-Related Health Effects. January 1981. IOM-81-01 (Tel. 202-389-6187).

Relates the impact of environmental hazards to costs of illness. Provides a framework for developing data bases and integrating exposure and cost estimates.

National Cancer Institute

Directory of Cancer Research Information Resources. International Cancer Research Data Bank. April 1981. 275 pp. NTIS-PB81-163537 ($8.50).

Multipurpose directory comprising a single volume listing of worldwide major accessible cancer information sources. Includes publications, registries, organizations, computer information services, and research projects information sources.

Organic Air Pollutants. March 1982. Office of the Scientific Coordinator, Division of Cancer Cause and Prevention, NCI, Bethesda, MD 20205.

Review of literature for organic chemicals reported to be potential airborne carcinogens.

National Center for Health Statistics

Environmental Health. A plan for collecting and coordinating statistical and epidemiological data. 1980. (PHS)80-1248 (Tel. 202-783-3738).

Reviews data bases for cross linkage of health and environmental information. Recommends ways of facilitating environmental health epidemiology and data collection efforts.

Environmental Health. A study of the issues in locating, assessing, and treating individuals exposed to hazardous substances. 1981. (PHS)81-1275.

Describes activities basic to the process of locating individuals who have been or may have been exposed to hazardous substances, determining the effect of such exposure on their health, and helping them to obtain access to appropriate treatment. Presents case studies and research recommendations.

Blood carbon monoxide levels in persons 3-75 years of age: United States, 1976-80. E.P. Radford and J.A. Drizd. March 17, 1982. Advancedata, No. 76. DHHS Pub. No. (PHS) 82-1250.

Blood lead levels for persons 6 months-74 years of age: United States, 1976-80. March 12, 1982. Advancedata, No. 79. DHHS Pub. No. (PHS) 82-1250.

National Commission on Air Quality

To Breathe Clean Air. 1981.

Analyzes and reports findings of the Congressional Commission regarding air pollution and public health.

National Heart, Lung, and Blood Institute

Report of the Working Group on Heart Disease Epidemiology, June 1979. NIH Publication No. 79-1667.

Indicates key areas of epidemiological research needed to increase understanding of cardiovascular diseases, their trends in the population, their precursors and causes, and optimal approaches to furthering disease control.

National Institute of Environmental Health Sciences

Environmental Health Perspectives (Editor, Environmental Health Perspectives, NIEHS, P.O. Box 12233, Research Triangle Park, NC 27709)

A bimonthly journal published to help give perspective to knowledge about the effect of environment on humans.

National Institute for Occupational Safety and Health (NIOSH)

Practical Problems and Policy Issues Arising from Exposures to Hazardous Chemical and Physical Agents in the Workplace. July 1977. 46 pp. NTIS-PB81-171050 ($6.50).

Implications of TSCA and OSHACT for workers and governmental Agencies.

National Technical Information Service (NTIS)

Cigarette Pollution Effects on Humans, January 1970-May 1981 (Citations from Pollution Abstracts). May 1981. 69 pp. NTIS PB81-866899 ($30.00).

Lists 66 citations dealing with health effects of primary and secondary exposure to cigarette smoke and other environmental pollutants. Economic considerations included.

Chronic Obstructive Lung Disease. 1964-1981, Citations from NTIS Data Base. March 1981. 83 pp. NTIS-PB81-804858 ($30.00).

Updated bibliography containing references on epidemiology, genetics and pathology of respiratory disease plus citations on effects of atmospheric pollutants and cigarette smoking.

Preventive Medicine: Hazardous Materials Exposure and Public Health. January 1976-November 1980. (Citations from Energy Data Base). NTIS-PB81-854838 ($30.00).

Bibliography contains citations related to prevention of health hazards associated with toxic substances in multiple environments.

National Telecommunications and Information Administration

Fifth Report on Program for Control of Electromagnetic Pollution of the Environment: The Assessment of Biological Hazards of Nonionizing Electromagnetic Radiation. March 1979. NTIS-79-19 (Tel. 202-724-3353).

Summarizes Federal research activities in nonionizing radiation especially related to exposure at low power densities over extended time periods.

National Toxicology Program

Annual Plan for FY1982. March 1982. NTP-81-94.

Presents accomplishments of FY1981 and planned efforts in toxicological testing, chemical selection, and information gathering.

Second Annual Report on Carcinogens. 1981. (To be available from NTIS)

Includes evidence for carcinogenicity, data on use, population exposure, and regulatory information on chemicals.

Office of Technology Assessment

Assessment of Technologies for Determining Cancer Risks from the Environment. OTA-H-138. June 1981. 242 pp. GPO-052-003-00832-1 (Tel. 202-783-3238).

Provides current review of important issues involving environmental carcinogens and cancer risks. Focuses on estimates of the percent of cancer due to environmental exposure, tests for determining carcinogenicity, data extrapolation methods, and regulatory policies and options.

Environmental Contaminants in Food. December 1979. GPO-052-003-00724-0 (Tel. 202-783-3238).

Delineates the major findings of an OTA investigation into chemical and radioactive contaminants of food. Proposes four options for Congress to consider including 1) maintaining existing system, 2) amending Food, Drug, and Cosmetic Act to permit tolerance setting after action levels , 3) establishing a national monitoring system, and 4) designating a lead Agency to coordinate Federal response to contamination problems.

Implications of Cost-Effectiveness Analysis of Medical Technology Summary. (Tel. 202-224-8996).

Presents findings on usefulness of cost-benefit analysis (CBA) and cost-effectiveness analysis (CEA) applied to medical technologies including R&D activities, HMO's, and health planning.

Radiation Policy Council (Council has been dissolved.)

Report of the Task Force on Occupational Radiation Exposure Regulation. August 1980.

Analyzes and evaluates the process for developing coordinated Federal policy for occupational exposures to ionizing radiation.

Report of the Task Force on Radon in Structures. August 1980.

Reviews the physical and biological evidence of radon exposures to the general public and makes recommendations concerning the Federal responses.

Toxicology Information Response Center (TIRC)

Health and Environmental Effects of Acid Rain. An Abstracted Literature Collection, 1966-1979. March 1980. 206 pp. NTIS-NLM/TIRC-80/1 ($17.00).

An abstracted bibliography containing 961 citations on acid rain effects plus a research directory listing information on current research projects.

Toxic Substances Strategy Committee

Toxic Chemicals and Public Protection. May 1980. GPO-0-318-148/6294 (Tel. 202-783-3238).

Presents findings and recommendations concerning the public health risks associated with toxic chemicals in the environment. Discusses policy research and regulatory activities designed to prevent and control toxic substances problems.

U.S. Department of Energy (DOE)

Acid Rain Information Book. Draft Final Report. GCA Corporation. December 1980. 229 pp. NTIS-DOE/EV/10273-1 ($18.50).

Presents a comprehensive review of acid rain phenomena and makes recommendations for future research.

Health Aspects of Nuclear Fuel and Waste Transport. S. Morris. 1979. (Tel. 301-353-3311).

A Suggested Bibliography for a Compendium of State of the Art Risk Assessment. W. Rowe. 1979. (Tel. 301-353-3311).

Radiation Risk Analysis. Resources for Future. 1980. (Tel. 202-252-4760).

National Health Assessment Methods. L. Hamilton and S. Morris. 1979. (Tel. 301-353-3311).

Comparative Assessment of Health and Safety Impacts of Coal Use. E. Salmon. 1980. (Tel. 301-353-4422).

U.S. Department of Health and Human Services

Promoting Health/Preventing Disease. Objectives for the Nation. 1980. Washington, D.C.: U.S. Government Printing Office.

Sets out specific and measurable objectives for 15 priority areas for achieving national health objectives.

U.S. Environmental Protection Agency

Asbestos/Asbestiform Research in EPA Office of Research and Development. JACA Corporation. March 1981. 93 pp. EPA-600/7-81-032; NTIS-PB81-191876 ($9.50).

A status report on EPA's research program on health effects of asbestos exposure.

Asbestos-Cement Materials Used in Water Supply. An Assessment of Current Information on the Occurrence and Question of Health Risk of Asbestos Fibers in Drinking Water Supplies. Health Effects Research Lab. (Cin.). April 1981. NTIS-PB81-196586 ($5.00).

Effects of Particulate Air Pollution on Asthmatic Subjects. National Asthma Center, Denver. April 1981. 83 pp. EPA-600/1-81-033; NTIS-PB81-190514 ($9.50).

Focuses on short-term health effects of air pollution, particularly sulfate and nitrate components of suspended particulates, on individuals with respiratory disease.

Health Effects Research and Standard Setting at EPA. SRI International. December 1980. 409 pp. NTIS-PB81-189698 ($29.00).

Evaluates the plans and programs in health-effects research at EPA and reviews how EPA identifies potential air pollutants for possible regulation.

Occupational Exposure to Ionizing Radiation in the United States: A Comprehensive Summary for the Year 1975. Office of Radiation Programs (J. Cook). November 1980. 152 pp. EPA-520/4-80-001; NTIS-PB81-172421 ($14.00).

Reports findings on radiation exposures in the workplace for the year 1975 in terms of dose levels and impacts.

Proceedings of the Research Planning Workshop on Health Effects of Oxidants Held at Raleigh, North Carolina on January 28-30, 1980. Health Effects Research Lab, (RTP). January 1981. 453 pp. EPA-600/9-81-001; NTIS-PB81-178832 ($32.00).

A compilation of presentations focusing on EPA-funded research in the Energy Interagency Health and Ecological Effects Program.

Report of Workshops on Epidemiologic Studies of Airborne Particulates Held at Research Triangle Park on April 3-4, 1980, and University of Pittsburgh on June 9-10, 1980. University of Pittsburgh (E. Radford). April 1981. 43 pp. EPA-600/1-81-039; NTIS-PB81-190480 ($6.50).

Presents the research recommendations developed concerning health effects of airborne particles.

Results of Research Related to Stratospheric Ozone Protection--Report to Congress. Office of Research and Development. October 1980. 58 pp. EPA-600/9-80-043; NTIS-PB81-176489 ($8.00).

Second EPA report (mandated by Clean Air Act) to Congress on research concerning ozone depletion and effects of increased ultraviolet exposure.

Appendix E

MEETING DATES

Working Group

September 16, 1981
January 20, 1982
March 3, 1982
April 19, 1982
May 27, 1982
July 1, 1982
July 28, 1982

Project Group on Exposure and Metabolic Mechanisms

January 8, 1982
March 23, 1982

Exposure Subcommittee

April 30, 1982
May 14, 1982
August 10, 1982

Metabolism Subcommittee

April 27, 1982

Project Group on the Standardization of Measurements and Tests

October 14, 1981

IEPLG

June 24, 1982

PROPOSED MEETING DATES FOR 1982-83

Meeting	Day and Date
Working Group	Thursday, September 23, 1982
Working Group	Thursday, November 4, 1982
Working Group	Thursday, January 27, 1983
Working Group	Thursday, March 24, 1983
Task Force Plenary	Thursday, April 14, 1983
Working Group	Thursday, May 26, 1983
Working Group	Thursday, June 30, 1983